[redacted]

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE SEBELA PATENT LITIGATION	Civil Action No.: 14-6414 (CCC) (MF)
	OPINION

CECCHI, District Judge.

I. INTRODUCTION

This is a consolidated[1] Hatch-Waxman patent infringement action brought by Plaintiff Sebela International Limited ("Sebela"). The Defendants in the consolidated action are Actavis Laboratories FL, Inc., Actavis Pharma, Inc., Andrx Corp., and Actavis, Inc.[2] (collectively, "Actavis"), and Prinston Pharmaceutical Inc., Solco Healthcare U.S., LLC, and Huahai US Inc. (collectively, "Prinston").

Plaintiff has asserted three patents against Defendants: U.S. Patent Nos. 7,598,271 (the "'271 patent"), 8,658,663 (the "'663 patent") and 8,946,251 (the "'251 patent"). A fourth patent, U.S. Patent No. 5,874,447 (the "'447 patent") was also asserted in this litigation. Sebela agreed to withdraw the claims related to the '447 patent in exchange for Defendants' agreement not to

[1] This case, docket number 14-6414, is the lead case in the consolidated action. The member cases are 15-6225, 14-7400, and 15-5308.

[2] Actavis, Inc. no longer exists in the same corporate form and is now known as Allergan Finance LLC. ECF No. 206, at 3 n.3.

launch their ANDA products until June 10, 2017, the expiration date of the '447 patent. ECF No. 175; SOF[3] ¶ 25.

The '271 patent is directed to a composition relating to Sebela's BRISDELLE® paroxetine mesylate product,[4] and the '663 and '251 patents (the "method of treatment patents") are directed to methods relating to the same. Noven Therapeutics, LLC ("Noven"), was the original holder of New Drug Application ("NDA") No. 204516 for paroxetine mesylate capsules, which are marketed and sold under the trademark BRISDELLE. SOF ¶ 8. On October 16, 2014, Noven sued Actavis for infringement of the '447, '271, and '663 patents. SOF ¶ 12. On August 14, 2015, Noven filed a second suit against Actavis for infringement of the '251 patent. SOF ¶ 13. On November 26, 2014, Noven sued Prinston for infringement of the '447, '271, and '663 patents. SOF ¶ 16. On July 7, 2015, Prinston sued Noven for declaratory judgment on the '251 patent. SOF ¶ 17. On July 25, 2016, Sebela purchased all benefits and interests in the '447, '271, '663, and '251 patents and NDA No. 204516 from Noven, and on September 20, 2016, Sebela was substituted as Plaintiff. SOF ¶¶ 21-24; ECF No. 155.

Defendants have sought approval from the United States Food and Drug Administration ("FDA") to market generic versions of paroxetine mesylate. SOF ¶¶ 71, 77. Plaintiff alleges that Defendants will infringe the patents in suit by marketing their generic products. Defendants have stipulated to infringement of the asserted claims of the '663 and '251 patents. SOF ¶¶ 49-50, 67-68.

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[3] SOF refers to the Stipulation of Facts agreed to by the Parties and adopted as part of the Final Pretrial Order, ECF No. 206.

[4] "Paroxetine mesylate" and "paroxetine methane sulfonate" are used variously to refer to the same compound. *See, e.g.*, 12/8 Tr. a.m. (Myerson) 87:18-21; 12/9 Tr. a.m. (Rogers) 29:3-11.

The Court conducted a bench trial in this matter from December 8, 2016, to December 14, 2016. The Parties submitted post-trial briefing and proposed findings of fact and conclusions of law. Closing arguments were held on February 24, 2017, and March 13, 2017. This Opinion constitutes the Court's findings of fact and conclusions of law pursuant to Federal Rule of Civil Procedure 52(a). The findings of fact are based on the Court's observations and credibility determinations of the witnesses who testified and a thorough review of all the evidence admitted at trial. For the reasons stated herein, the Court finds as follows:

As to the '271 patent, Plaintiff has not met its burden of proving infringement by a preponderance of evidence, so judgment of non-infringement will be entered in favor of Defendants on the '271 patent.[5]

As to the '663 patent, Defendants have met their burden of proving by clear and convincing evidence that the '663 patent is invalid, so judgment of invalidity will be entered in favor of Defendants on the '663 patent.

As to the '251 patent, Defendants have met their burden of proving by clear and convincing evidence that the '251 patent is invalid, so judgment of invalidity will be entered in favor of Defendants on the '251 patent.

II. BACKGROUND[6]

A. Parties

Plaintiff Sebela is a Bermuda company with offices located in Hamilton, Bermuda. SOF ¶ 1. Sebela is the legal owner of all rights, title and interests in the '271, '663, and '251 patents.

[5] As discussed below, the Court has not reached the issue of invalidity as to the '271 patent given Defendants' presentation of the claim in the alternative and the representations that this issue is amenable to resolution.

[6] Certain findings of fact are also provided in connection with the Court's conclusions of law.

SOF ¶¶ 31, 40, 54. Sebela Ireland Ltd., a wholly owned subsidiary of Sebela, holds NDA No. 204516. SOF ¶ 22.

Defendant Actavis Laboratories FL, Inc. is a Florida corporation with a place of business at Morris Corporate Center III, 400 Interpace Parkway, Parsippany, New Jersey 07054. SOF ¶ 2. Defendant Actavis Pharma, Inc. is a Delaware corporation with a place of business at Morris Corporate Center III, 400 Interpace Parkway, Parsippany, New Jersey 07054. SOF ¶ 3. Defendant Andrx Corp. is a Delaware corporation with a place of business at 4955 Orange Drive, Davie, Florida 33314. SOF ¶ 4. Defendant Actavis submitted Abbreviated New Drug Application ("ANDA") No. 207129 to the FDA, including a paragraph IV certification as to each of the patents in suit. SOF ¶ 11.

Defendant Prinston Pharmaceutical Inc. is a corporation organized and existing under the laws of Delaware with a principal place of business at 2002 Eastpark Boulevard, Cranbury, New Jersey 08512. SOF ¶ 5. Defendant Solco Healthcare U.S., LLC is a Delaware corporation with a principal place of business at 2002 Eastpark Boulevard, Suite A, Cranbury, New Jersey 08512. SOF ¶ 6. Defendant Huahai US Inc., is a corporation organized and existing under the laws of New Jersey, with a place of business at 2001 Eastpark Boulevard, Cranbury, New Jersey 08512. SOF ¶ 7. Defendant Prinston filed ANDA No. 207188 with the FDA, identifying the BRISDELLE drug product, and seeking to market and sell within the United States a generic 7.5 mg paroxetine mesylate capsule product. SOF ¶ 14. ANDA No. 207188 contains a paragraph IV certification as to each of the patents in suit. SOF ¶ 15.

B. Patents in Suit

i. The '271 Patent

The '271 Patent, titled "Crystalline Paroxetine Methane Sulfonate," issued on October 6, 2009 (with certificates of correction issued on May 17, 2011, and December 22, 2015), from U.S.

Application Serial No. 09/200,743 (the "'743 application"), which was filed on November 30, 1998. SOF ¶ 27. The '743 application was filed as a divisional of U.S. Application Serial No. 08/872,023 (the "'023 application"), which was filed on June 10, 1997, and issued as the '447 patent. SOF ¶ 27. The '743 application included a priority claim to the '023 application. SOF ¶ 27. The '271 patent relates generally to a crystalline form of paroxetine mesylate. SOF ¶ 35; JTX-2. The inventors listed on the '271 patent are Franciscus Bernardus Gemma Benneker, Frans Van Dalen, Jacobus Maria Lemmens, Theodorus Hendricus Antonium Peters, and Frantisek Picha. SOF ¶ 30; JTX-2.

On January 31, 2001, Synthon, which was the holder of the '743 application, filed a request for an interference between the '743 application and U.S. patent No. 6,063,927 (the "'927 patent"), which was owned by SmithKline Beecham and claimed a crystalline form of paroxetine mesylate described by reference to 8 infrared ("IR") peaks. PFOF[7] ¶¶ 55, 62; DFOF[8] ¶ 102. The patent examiner suspended prosecution of the '743 application on February 21, 2001, PFOF ¶ 64, and the Board of Patent Appeals and Interferences (the "BPAI") instituted an interference proceeding (the "Interference Proceeding") on October 1, 2002, PFOF ¶ 67. Despite the different peak listings, applying the broadest reasonable interpretation standard, the BPAI ultimately decided the interference in Synthon's favor. *See* PFOF ¶ 77.

ii. The Method of Treatment Patents

The '663 patent, titled "Method of Treating Thermoregulatory Dysfunction with Paroxetine," issued on February 25, 2014 (with a certificate of correction issued on October 7, 2014), from U.S Application Serial No. 12/292,960 (the "'960 application"). The '960 application

[7] PFOF refers to Plaintiff's Proposed Findings of Fact and Conclusions of Law, ECF No. 226.

[8] DFOF refers to Defendants' Proposed Findings of Fact and Conclusions of Law, ECF No. 217.

was filed on December 1, 2008, as a continuation of the now abandoned U.S. Application Serial No. 11/499,586 (the "'586 application"), which was filed on August 4, 2006. SOF ¶ 36; JTX-3. The '633 patent relates generally to methods of using paroxetine to treat thermoregulatory dysfunction. *See* SOF ¶¶ 46-48; JTX-3. The sole inventor listed on the '663 patent is Patricia Allison Tewes Richards. SOF ¶ 39; JTX-3.

The '251 patent, also titled "Methods of Treating Thermoregulatory Dysfunction with Paroxetine," issued on February 3, 2015, from U.S. Application Serial No. 14/157,992 (the "'992 application"), which was filed on January 17, 2014. SOF ¶ 51. The '992 application was a continuation of the '960 application. SOF ¶ 51; JTX-4. The '251 patent relates generally to methods of using paroxetine to treat thermoregulatory dysfunction. *See* SOF ¶¶ 62-66; JTX-4. The sole inventor listed on the '251 patent is Patricia Allison Tewes Richards. SOF ¶ 53; JTX-4.

The specifications of the '663 patent and the '251 patent are substantively identical.[9] PFOF ¶ 207; DFOF ¶ 26. The specifications disclose that paroxetine can be used to treat hot flashes at doses of 9.5 mg down to 0.1 mg. 12/12 Tr. a.m. (Locker) 91:5-11. The specifications contain two prophetic examples. 12/12 Tr. a.m. (Locker) 91:12-92:3. Example 1 describes administering paroxetine hydrochloride and paroxetine mesylate at doses of 1.0, 2.0, 3.0, 4.0, 5.0, 6.0, 7.0, 8.0, and 9.5.[10] DFOF ¶ 14; JTX-3 at 4:63-5:23. Example 2 describes administering paroxetine hydrochloride, in anhydrous form, hemihydrate form, and monohydrate form, at doses of 1.0, 2.0, 3.0, 4.0, 5.0, 6.0, 7.0, 8.0, 9.0, and 9.5. DFOF ¶ 15; JTX-3 at 5:25-6:23. In each example the patent concludes that "[a]fter a few days to weeks, the symptoms ameliorate." DFOF ¶ 15; JTX-3 at 5:23, 6:23.

[9] Except where necessary for the purposes of clarity, the Court will cite to the specification of the '663 patent.

[10] Based on the context in the specification, the Court assumes these values are in mg/day.

C. Trial Witnesses

The following witnesses appeared and provided live testimony during the bench trial:

i. Plaintiff's Fact Witness

1. Scott Briggs

The Court heard testimony from Mr. Scott Briggs, who is Chief Commercial Officer at Sebela Pharmaceutical, Inc., 12/13 Tr. (Briggs) 17:12, and who previously served as Vice President of Marketing and Sales at Noven, 12/13 Tr. (Briggs) 18:12-13. Mr. Briggs testified on issues related to the marketing and sales of Brisdelle.

ii. Plaintiff's Expert Witnesses

1. Allan Myerson

The Court heard expert testimony from Allan Myerson, Ph.D. The Court accepted Dr. Myerson as an expert in the fields of crystallization, crystal and solid forms, pharmaceutical manufacturing, and industrial applications of crystallization. 12/8 Tr. a.m. (Myerson) 86:23-87:6. Dr. Myerson opined on the issues of infringement of the '271 patent and validity of the method of treatment patents.

2. John C. Jarosz

The Court heard expert testimony from John C. Jarosz. The Court accepted Mr. Jarosz as an expert in the fields of pharmaceutical economics and economic issues regarding secondary considerations of commercial success. 12/13 Tr. (Jarosz) 67:18-68:1. Mr. Jarosz opined on the issues related to the market performance of Brisdelle.

3. James A. Simon

The Court heard expert testimony from James A. Simon, M.D. The Court accepted Dr. Simon as an expert on the clinical treatment, clinical research and management of the symptoms and medical consequences of menopause, including vasomotor symptoms. 12/13 Tr. (Simon)

117:23-118:7. Dr. Simon opined on issues related to the validity of the method of treatment patents.

4. James R. Woodworth

The Court heard expert testimony from James R. Woodworth, Ph.D. The Court accepted Dr. Woodworth as an expert in the field of pharmacokinetics, pharmacodynamics, and clinical pharmacology. 12/14 Tr. (Woodworth) 115:6-14. Dr. Woodworth opined on issues related to the validity of the method of treatment patents.

iii. Defendants' Expert Witnesses

1. Robin D. Rogers

The Court heard expert testimony from Robin D. Rogers, Ph.D. The Court accepted Dr. Rogers as an expert in the field of "solid state chemistry, including crystal engineering, crystallization, crystal characterization, including by IR spectroscopy, salts and polymorphism, including the isolation and characterization of organic compounds and their applications in pharmaceutical products." 12/9 Tr. a.m. (Rogers) 23:22-24:8. Dr. Rogers opined on the issues of infringement and invalidity of the '271 patent.

2. Brian K. Locker

The Court heard expert testimony from Brian K. Locker, M.D. The Court accepted Dr. Locker as an expert in treating women with thermoregulatory dysfunction associated with hot flashes. 12/12 Tr. a.m. (Locker) 87:5-13. Dr. Locker opined on the issue of validity of the method of treatment patents.

3. Ivan T. Hoffman

The Court heard expert testimony from Ivan T. Hoffman CPA/CFF, CLP. The Court accepted Mr. Hoffman as an expert in the field of pharmaceutical economics. 12/14 Tr. (Hoffman) 167:9-18. Mr. Hoffman opined on the issues related to the market performance of Brisdelle.

iv. Deposition videos

The following witnesses had video recordings of portions of their depositions played during the bench trial:

1. Theodorus Hendricus Antonium Peters

The Court saw video testimony from Dr. Theodorus Hendricus Antonium Peters, one of the named inventors of the '271 patent.

2. Patricia Tewes Richards

The Court saw video testimony from Dr. Patricia Tewes Richards the named inventor of the method of treatment patents.

3. Joel Lippman

The Court saw video testimony from Dr. Joel Lippman, the Chief Medical Officer of and a 30(b)(6) witness for Noven.

D. Confidential Prosecution Documents

Defendants have sought to introduce documents from the confidential record of the Interference Proceeding. Specifically, they seek to introduce expert declarations filed by Drs. Harry G. Brittain (DTX-14B) ("Brittain Declaration") and Wayne Genck (DTX-14C) ("Genck Declaration"), and excerpts from deposition testimony given by Dr. Bennecker in a proceeding in the United Kingdom (PTX-880) ("Bennecker Deposition").[11] ECF No. 249. On the eve of trial, the Parties informed the Court that Plaintiff objected to Defendants' use of these documents on a number of grounds. Among other things, Plaintiff challenged the authenticity of these documents on the grounds that, although they were produced by Sebela on behalf of its predecessor Synthon,

[11] Initially, the Parties disputed the admissibility of more documents from the confidential record, but since the trial, the Parties appear to have focused the dispute on these three documents. *See* ECF No. 265 at 1.

see ECF No. 270 at 2, which had maintained them in its records, they were not official, certified copies. During the course of the bench trial, the Court allowed these materials to be presented and discussed by the Parties, reserving judgment on their admissibility. Prior to closing arguments, the Parties submitted briefing on the admissibility of these documents. ECF Nos. 219, 221, 229, 235. At closing arguments, it became clear that none of the Parties had actually attempted to obtain certified copies of the documents from the Patent and Trademark Office ("PTO"), so the Court advised the Parties do so. On May 1, 2017, over a month after closing arguments, Defendants produced a copy of the certified interference file history, containing the disputed documents including the Brittain Declaration, Genck Declaration, and Bennecker Deposition. ECF No. 265. In a May 8, 2017 letter Plaintiff objected to this production as untimely and argued that its consideration would not be appropriate as the certified copies of the documents were not in evidence at the time of trial. ECF No. 270.

The interference documents are part of the file history of the '271 patent. While Plaintiff argued at trial that the confidential documents at issue are not part of the file history because "[w]hen you obtain a certified copy it will not include the confidential [documents]," 3/13 Tr. 183:8-12, this is clearly not the case, as the certified record produced by Defendants includes the disputed confidential documents. Given the dilatory conduct giving rise to this issue, [12] and the normal amount of time it takes to obtain a certified file history, the Court will consider the certified

[12] The Court notes that while Local Patent Rule 3.2(c) does not expressly require the early production of the entirety of the file history if it is not in the plaintiff's possession, Rule 3.2(c) indicates a strong policy in favor of the early production of the complete file history. The Court is surprised that a timely production of the entire file history appears to have not occurred in this case and that the matter was raised with the trial court just days before the trial, particularly given the sophistication of the parties in this case. Considerable time and resources have been expended by the Parties and the Court in addressing questions of authenticity and completeness, which certainly could have been resolved much earlier in this litigation.

file history. Furthermore, the production of the certified copies of the disputed documents merely confirms the authenticity of the copies that were, in fact, offered at trial. *See* Fed. R. Evid. 104(a). Accordingly, Plaintiff's general objections to the consideration of these documents is overruled. Objections specific to particular materials are considered below.

E. Scientific Principles

The patents in suit involve crystal forms of compounds, infrared spectroscopy, and the treatment of thermoregulatory disorders. The following is an introduction to some of the scientific principles at issue in this litigation.

i. Crystals and Polymorphism

Paroxetine is a compound that has pharmaceutical uses, including as an antidepressant and, as claimed in the patents in suit, as a drug for treating thermoregulatory dysfunction. *See, e.g.*, JTX-4 1:51-58. Paroxetine can form a variety of salts, including paroxetine mesylate, also known as paroxetine methanesulfonate. *See, e.g.*, JTX-1 at 1:27-33.

Several of the patent claims at issue relate to different chemical forms of paroxetine and the arrangement of the molecules therein. When the molecules are arranged in an ordered, repeating, regular pattern, they are said to be in a crystalline form. *See* 12/8 Tr. a.m. (Myerson) 89:8-17; *cf.* 12/9 Tr. a.m. (Rogers) 25:14-15. In contrast, when the molecules are not in an ordered array, they are said to be in an amorphous form. *See, e.g.*, 12/8 Tr. a.m. (Myerson) 90:1-6; 12/9 Tr. a.m. (Rogers) 25:14-15. In general, amorphous forms of a compound are less chemically stable and less physically stable than crystalline forms, so crystalline forms are often preferred for pharmaceutical use. *See, e.g.*, 12/8 Tr. a.m. (Myerson) 90:9-15.

Certain molecules have more than one repeating pattern, or crystalline form, into which they can be arranged. Each of the crystalline forms is referred to as a polymorph. 12/8 Tr. a.m. (Myerson) 92:14-18; 12/9 Tr. a.m. (Rogers) 26:10-22. Although made up of the same constituent

molecules, polymorphs can have different physical and chemical properties that are pharmaceutically significant, including physical stability, solubility, and dissolution. 12/8 Tr. a.m. (Myerson) 92:24-93:3; *see also* 12/9 Tr. a.m. (Rogers) 26:25-27:9. When a compound has only one crystalline form, it may be referred to as "monomorphic." 12/9 Tr. p.m. (Rogers) 70:1-4.

Polymorphism is unpredictable. 12/8 Tr. a.m. (Myerson) 94:12-95:2; *see also* 12/9 Tr. p.m. (Rogers) 56:20-57:1. Although compounds with molecular weights below a certain threshold can usually be crystallized with sufficient effort, 12/8 Tr. a.m. (Myerson) 95:10-20 ("[T]ypically for compounds with molecular weights below 1500 [Daltons], if you work on them long enough you can usually get them to crystallize . . . ."[13]), it is not possible to predict how many polymorphs may exist for a given compound, 12/8 Tr. a.m. (Myerson) 95:21-96:1; 12/8 Tr. p.m. (Myerson) 5:23-6:1; *see also* 12/9 Tr. p.m. (Rogers) 51:2-12. A new polymorph may take decades to be discovered. 12/8 Tr. p.m. (Myerson) 7:5-17; 12/9 Tr. p.m. (Rogers) 53:3-10.

ii. Infrared Spectroscopy

Crystalline forms may be characterized and described using IR spectroscopy. IR spectroscopy involves shining IR radiation at a sample of the compound. Certain frequencies of radiation are absorbed by the sample as they interact with it. 12/9 Tr. a.m. (Rogers) 32:24-33:9. Which frequencies are absorbed depends on the properties of the sample, including the crystalline structure. A spectrum can be generated by plotting absorption versus IR frequency. Peaks are observed in the spectrum at those frequencies where the light was absorbed by, and therefore did not pass through, the sample. 12/8 Tr. a.m. (Myerson) 101:24-102:5, 104:10-15. These peaks can be used to characterize the crystalline form. 12/8 Tr. a.m. (Myerson) 102:10-13. These peaks may

[13] The molecular weight of paroxetine mesylate is 425.5 Daltons. PTX-0977.0002; *see also* 12/8 Tr. a.m. (Myerson) 99:21-100:4.

be sharp or weak. 12/8 Tr. p.m. (Myerson) 22:3-8, 22:23-23:7. Typically, IR spectra are measured in units of reciprocal centimeters, also called wavenumbers. 12/8 Tr. a.m. (Myerson) 104:10-15. Often there is a greater number of peaks between 500 cm^{-1} and 1500 cm^{-1}, and this region on the spectrum is referred to as the "fingerprint region." 12/8 Tr. a.m. (Myerson) 104:16-19; 105:8-12.

There are several ways in which variation can be introduced into the measurement of peaks. These include differences in the instruments used to generate the spectra, 12/8 Tr. a.m. (Myerson) 105:17-18; 12/9 Tr. p.m. (Rogers) 40:21-22, calibration of the instrument used, 12/8 Tr. a.m. (Myerson) 105:18-23, and sample preparation (e.g., mixture of the sample with a salt, size of the grains of the powder, concentration of the powder on the disk, use of an oil mull), 12/8 Tr. a.m. (Myerson) 105:24-106:14; 12/9 Tr. p.m. (Rogers) 40:24-25. Instrument resolution can also alter the ability to distinguish peaks and can affect how the peaks look and their apparent location. 12/8 Tr. a.m. (Myerson) 107:1-13; *see also* 12/9 Tr. p.m. (Rogers) 41:7-9. If a low resolution is used, fewer peaks will be observed, and separate peaks may merge into a single peak which may affect apparent location. 12/8 Tr. a.m. (Myerson) 108:15-23. Typically, a resolution of 1 cm^{-1}, 2 cm^{-1}, or 4 cm^{-1} is used. 12/8 Tr. a.m. (Myerson) 109:12-19.

The method used for identifying and locating peaks can also introduce variability in the measured value. 12/9 Tr. p.m. (Rogers) 41:3-6. Peak-picking software can use various algorithms to determine whether something is a peak and the location of the peak. 12/8 Tr. a.m. (Myerson) 106:15-20. Most instruments come with a default setting for identifying peaks and allow the user to adjust the settings to be more or less sensitive. 12/8 Tr. a.m. (Myerson) 106:21-25. Peak-picking software was available and in use as of 1995. 12/8 p.m. Tr. (Myerson) 4:19-21.

In order to reduce "noise," or variability due to factors other than the sample, a person of ordinary skill in the art ("POSA")[14] will typically run a number of scans, and then "co-add" those scans, to increase the signal to noise ratio. 12/8 p.m. Tr. (Myerson) 16:22-17:2. Typically, a POSA will perform 32 to 64 co-added scans. 12/8 Tr. p.m. (Myerson) 60:19-24, 61:18-62:2.

Typically, the differences between peaks that a POSA would look for in distinguishing between two different polymorphs of the same compound are around 4 cm^{-1}. 12/8 Tr. p.m. (Myerson) 72:5-10. It is possible, though unlikely, however, that a polymorph has an IR peak that is more than 18 cm^{-1} away from a corresponding peak in a different polymorph of the same compound. 12/8 Tr. p.m. (Myerson) 72:23-73:4, 103:16-19. While IR spectroscopy can always be used to distinguish between samples with different underlying chemical structures, it cannot always be used to distinguish between polymorphs. 12/8 Tr. p.m. (Myerson) 71:18-23. Instead, there are many instances where IR spectroscopy cannot distinguish between polymorphs. 12/8 Tr. p.m. (Myerson) 72:1-4. Accordingly, while IR spectroscopy is commonly used for identifying chemical species, it is only occasionally used by itself to distinguish between different crystalline forms. 12/8 Tr. p.m. (Myerson) 90:22-91:9; 12/9 Tr. a.m. (Rogers) 32:14-22.

There are several additional methods by which crystalline forms may be characterized. These include single crystal x-ray diffraction, 12/8 Tr. a.m. (Myerson) 96:19-23, powder x-ray diffraction ("XRPD"), 12/8 Tr. a.m. (Myerson) 96:24-97:4; 12/9 Tr. a.m. (Rogers) 32:14-21, and phase transition analysis, such as by differential scanning calorimetry ("DSC"), 12/8 Tr. a.m. (Myerson) 97:12-98:8; 12/9 Tr. a.m. (Rogers) 32:11-13. Each of these methods was available to a POSA in 1997. 12/8 Tr. a.m. (Myerson) 99:1-3; *see* 12/9 Tr. p.m. (Rogers) 53:11-13. Unlike

[14] In this Opinion, the Court will refer to a person of ordinary skill in the art as a "POSA." This term includes all iterations of this concept, such as "a person having ordinary skill in the art," "one of ordinary skill in the art," etcetera.

IR spectroscopy, XRPD will provide virtually conclusive evidence informing a POSA what polymorph is being analyzed. 12/8 Tr. p.m. (Myerson) 70:20-23. Accordingly, IR spectroscopy is not used nearly as often as XRPD to distinguish between crystalline forms. *See* 12/8 Tr. p.m. (Myerson) 70:18-72:4; 12/9 Tr. a.m. (Rogers) 32:14-22.

iii. Thermoregulatory Disorders

Thermoregulatory dysfunction refers to the dysfunction of a body's ability to control its temperature. 12/12 Tr. a.m. (Locker) 84:6-11. This typically occurs during menopause. 12/12 Tr. a.m. (Locker) 84:8-11. The main symptoms associated with thermoregulatory dysfunction are hot flashes or hot flushes and night sweats. 12/12 Tr. a.m. (Locker) 84:12-13; 12/13 Tr. (Simon) 119:2-8. Hot flashes, or thermoregulatory dysfunction generally, may also be referred to as vasomotor symptoms. 12/12 Tr. a.m. (Locker) 89:21-23; 12/13 Tr. (Simon) 119:9-11. The precise cause of vasomotor symptoms is unknown. 12/13 Tr. (Simon) 121:17-19; 12/14 Tr. (Simon) 12:10-14. Sixty to eighty percent of menopausal women experience vasomotor symptoms, and approximately one in five seek medical treatment for those symptoms. 12/13 Tr. (Simon) 119:16-22.

F. Background of the Claimed Inventions

i. Development of Crystalline Paroxetine Mesylate

In the late 1990s, researchers at Synthon developed a crystalline form of paroxetine mesylate. *See* PTX-801.0003; JTX-1 at 7:45-60. Paroxetine mesylate is a salt in which the active component is the paroxetine base. Dr. Benneker, a researcher at Synthon, analyzed the crystalline form of paroxetine mesylate that had been developed and generated a list of IR peaks, the peaks now listed in claim 1 of the '271 patent. *See* PTX-801.0003.

The spectrum used to identify the listed peaks was included in the prosecution history of the '271 patent. The spectrum had a resolution of 8 cm^{-1}, rather than the standard 1 cm^{-1} to 4 cm^{-1}.

12/8 Tr. a.m. (Myerson) 107:22-25, 109:12-19. At high transmission areas, the spectrum appears to show a high degree of variability in the signal due to factors other than the sample, a problem that would often be addressed by co-adding scans. 12/8 Tr. p.m. (Myerson) 16:5-17:2. The intrinsic record does not appear to indicate how many co-added scans Dr. Benneker performed. 12/8 Tr. p.m. (Myerson) 62:7-11.

During the Interference Proceeding, Dr. Benneker submitted a declaration describing how he measured the peaks from an IR spectrum he had generated. PTX-801 ("Benneker Declaration"); *see also* 12/8 Tr. p.m. (Myerson) 18:1-21:22. He did not use a peak-picking algorithm to generate the list of claimed peaks in the '271 patent. Instead, he measured the peaks by hand with a ruler. 12/8 Tr. a.m. (Myerson) 107:17-21. Dr. Benneker stated that he "calculated the wavenumber for each peak by measuring with a ruler the distance between the wavenumbers marked on the X-axis." PTX-801.0004. He further stated that "[t]he measurements were made approximately to the nearest 0.5 mm." PTX-0801.0004. The Benneker Declaration further explained that he used these measurements to calculate a scale factor. He then "placed the ruler parallel to the Y-axis . . . directly against the side of the peak to be measured and marked this point on the X-axis." PTX-801.0004. Finally, he measured the distance "approximately to the nearest 0.5 mm" from the closest wavenumber marked on the X-axis to the marked point on the X-axis and used this measurement to calculate the peak's location. PTX-801.0004.

To date, the crystalline form of paroxetine mesylate studied by Dr. Benneker is the only polymorphic form that has been found. 12/8 Tr. p.m. (Myerson) 9:21-10:3. In seeking to institute the Interference Proceeding, Synthon affirmatively represented to the PTO that "[a]ll of the evidence . . . indicates that there is only a single crystalline form of paroxetine [mesylate]." JTX-6. Although it is theoretically possible that another crystalline form of paroxetine mesylate will be

discovered in the future, 12/8 Tr. p.m. (Myerson) 10:17, Dr. Rogers testified that "it is highly unlikely" that another form would be found. 12/9 Tr. a.m. (Rogers) 96:7-20. In reaching his conclusion, Dr. Rogers considered the Genck Declaration and the Brittain Declaration, which describe a polymorph screen in which Dr. Genck attempted crystallization of paroxetine mesylate under thousands of different sets of conditions. *See* 12/9 Tr. a.m. 89:24-91:20. Only one form was found and Dr. Genck concluded that paroxetine mesylate was not polymorphic. 12/9 Tr. a.m. 91:15-20.[15]

ii. Development of the Method of Treatment Patents

The method of treatment patents claim uses of paroxetine to treat vasomotor symptoms. The asserted claims of the '663 patent are directed to the use of the mesylate salt of paroxetine, *i.e.*, paroxetine mesylate, while the asserted claims of the '251 patent are directed more generally to any pharmaceutically acceptable salt of paroxetine. Paroxetine belongs to a class of antidepressants known as selective serotonin reuptake inhibitors ("SSRIs"). Paroxetine hydrochloride is a salt of paroxetine that has been used commercially to treat depression since 1997, under the name Paxil. 12/12 Tr. a.m. (Locker) 93:7-13.

[15] While Plaintiff asserts that these declarations consist of hearsay, there is no dispute that the studies described in them "were reasonable studies." 12/8 Tr. p.m. (Myerson) 12:18-20. The Court finds that Dr. Roger's testimony was permissible under Federal Rule of Evidence 703. *See O2 Micro Int'l Ltd. v. Monolithic Power Sys., Inc.*, 420 F. Supp. 2d 1070, 1088 (N.D. Cal. 2006) ("Rule 703 allows an expert to rely on facts or data relied upon by experts in the particular field in forming opinions or inferences upon the subject; an expert is not required to testify only upon data the expert has personally gathered or tested."), *aff'd*, 221 F. App'x 996 (Fed. Cir. 2007). Defendants have presented several other grounds for considering this testimony. Specifically, they have argued that the testimony constitutes an admission by a party opponent under Rule 801(d)(2)(D), or an adopted admission under 801(d)(2)(B). They also argue that it is admissible as prior deposition testimony under Rule 804(b)(1) or is admissible under the Rule of Completeness.

Vasomotor symptoms have long been treated with hormone therapy. *See, e.g.*, 12/13 Tr. (Simon) 123:4-10. However, a large part of the population of women needing treatment are unable to take hormone therapy for vasomotor symptoms, including patients who are suffering from or at risk of developing breast cancer. 12/12 Tr. p.m. (Locker) 25:5-14; 12/13 Tr. (Simon) 123:11-22. Starting in the 1960s, researchers evaluated the efficacy of various non-hormonal treatments. 12/13 Tr. (Simon) 126:1-127:17. In the 1990s, researchers were assessing the use of a variety of antidepressants for the treatment of vasomotor symptoms, including venlafaxine (a serotonin-norepinephrine reuptake inhibitor, or "SNRI"), paroxetine, sertraline, fluoxetine, citalopram, and mirtzapine. 12/13 Tr. (Simon) 127:20-134:20. All of these agents were being tested at the antidepressant dose or higher. 12/13 Tr. (Simon) 135:6-9. An additional compound, gabapentin, also indicated efficacy during this period. 12/13 Tr. (Simon) 136:21-137:5.

In 2000, a pilot study published by Stearns, *et al.*, established that paroxetine hydrochloride was effective to treat hot flashes at doses as low as 10 mg/day. *See* 12/12 Tr. a.m. (Locker) 90:9-18, 94:7-25; JTX-33). In 2004, a patent application filed by Lemmens, *et al.*, concluded that paroxetine mesylate was preferable to paroxetine hyrdrochloride as it is more highly water soluble and has better thermal stability. 12/12 Tr. a.m. (Locker) 93:17-23; PTX-983. In 2005, a more sophisticated study was published on 10 mg and 20 mg doses of paroxetine. 12/12 Tr. a.m. (Locker) 95:14; JTX-34. The second study also indicated that there was a decrease in negative side effects from the 20 mg dose to the 10 mg dose. 12/12 Tr. a.m. (Locker) 97:21-98:5. By 2005, doctors were prescribing 10 mg doses of Paxil off-label for treatment of hot flashes, 12/12 Tr. a.m. (Locker) 98:19-99:7, and doctors were using other SSRIs and SNRIs to treat hot flashes. 12/12 Tr. a.m. (Locker) 97:15-20.

In 2002, the Women's Health Initiative ("WHI") study was published. This was a major study that clearly demonstrated increased risk of several serious conditions, including breast cancer, stroke and heart attacks, as a result of hormonal treatments. 12/13 Tr. (Simon) 124:24-125:6. This led to an increased focus on developing non-hormonal treatments for vasomotor symptoms. 12/13 Tr. (Simon) 125:16-20. However, SSRIs and SNRIs, and paroxetine in particular, have a number of side effects associated with them, including weight gain and sexual dysfunction, which are particularly problematic for menopausal women. 12/12 Tr. p.m. (Locker) 30:16-31:21; 12/13 Tr. (Simon) 141:22-143:4. Furthermore, at the time of the invention, tamoxifen was a commonly prescribed breast cancer therapy, 12/12 Tr. p.m. (Locker) 25:19-26:4; 12/13 Tr. (Simon) 144:1-16, and paroxetine was known to interfere with the efficacy of tamoxifen. 12/12 Tr. p.m. (Locker) 26:5-20; 12/13 Tr. (Simon) 144:17-20.

Dr. Richards, the named inventor on the method of treatment patents, testified that she had experience prescribing low doses of antidepressants to treat pain, Richards Dep. 53:11-16, 53:20-54:6, knowledge that there is thermoregulatory function in the hypothalamus, and knowledge that there are serotonergic neurons in the hypothalamus. Richards Dep. 57:1-58:13. Based on this, she concluded that paroxetine mesylate "could" work in treating hot flashes. Richards Dep. 57:1-58:13.

G. The Products at Issue

i. Plaintiff's BRISDELLE® Products

Noven was the original holder of NDA No. 204516 for paroxetine mesylate capsules, which are marketed and sold under the registered trademark BRISDELLE. SOF ¶ 8. Paroxetine mesylate is the active ingredient in BRISDELLE. SOF ¶ 26. BRISDELLE is FDA indicated for the treatment of moderate to serve vasomotor symptoms associated with menopause. Each

BRISDELLE capsule contains 9.69 mg paroxetine mesylate, equivalent to 7.5 mg paroxetine base. SOF ¶ 9.

On July 25, 2016, Sebela purchased all benefits and interests in the '447, '271, '663, and '251 patents, and NDA No. 204516. SOF ¶ 21. NDA No. 204516 is held by Sebela Ireland Ltd., a wholly owned subsidiary of Sebela. SOF ¶ 22.

ii. Defendants' ANDA Products

1. Actavis

Actavis Laboratories FL, Inc. submitted ANDA No. 207139 to the FDA under Section 505(j) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 505(j), seeking FDA approval to engage in the commercial manufacture, use, or sale of 7.5 mg paroxetine mesylate capsules. SOF ¶ 71. ANDA No. 207139 contains certifications pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV), *i.e.*, Paragraph IV certifications, alleging that the claims of the patents in suit are invalid, unenforceable, and/or will not be infringed by the commercial manufacture, use, or sale of the proposed drug products that are the subject of Actavis' ANDA No. 207139. SOF ¶¶ 11, 72. The active pharmaceutical ingredient in Actavis' ANDA Product is paroxetine mesylate. SOF ¶ 73.

2. Prinston

Prinston Pharmaceutical, Inc. submitted ANDA No. 207188 to the FDA under Section 505(j) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 505(j), seeking FDA approval to engage in the commercial manufacture, use, or sale of 7.5 mg paroxetine mesylate capsules. SOF ¶ 77. ANDA No. 207188 contains Paragraph IV certifications, alleging that the claims of the patents in suit are invalid, unenforceable, and/or will not be infringed by the commercial manufacture, use, or sale of the proposed drug products that are the subject of Prinston's ANDA No. 207188. SOF ¶¶ 15, 78. The active pharmaceutical ingredient in Prinston's ANDA Product is paroxetine mesylate. SOF ¶ 79.

III. ISSUES TO BE DECIDED

Plaintiff has asserted the following claims against Defendants:

'271 patent: Claim 1. SOF ¶ 32.

'663 patent: Claims 1, 2, and 5. SOF ¶ 41.

'251 patent: Claims 1, 2, 4, 9, and 10. SOF ¶ 55.

Defendants have stipulated to infringement of the asserted claims of the '663 and '251 patents. SOF ¶¶ 49-50, 67-68. Defendants contend the asserted claim of the '271 patent is not infringed, or alternatively, is invalid, SOF ¶ 33. Defendants further contend that the asserted claims of the '663 patent are invalid, SOF ¶ 42, and the asserted claims of the '251 patent are invalid, SOF ¶ 56.

The following issues are before the Court:

A. '271 Patent – Infringement

Plaintiff alleges that Defendants' ANDA products will directly infringe the sole claim of the '271 patent under 35 U.S.C. § 271(a). Defendants dispute Plaintiff's claim of infringement.

B. '271 Patent – Invalidity

Although Defendants contest infringement, they alternatively argue that if claim 1 of the '271 patent is found to be infringed, that claim is invalid under the doctrine of obviousness-type double patenting and invalid as obvious under 35 U.S.C. § 103.

C. '663 Patent – Invalidity

Defendants allege that the asserted claims of the '663 patent are invalid pursuant to 35 U.S.C. §§ 101 & 112 for lack of utility, invalid pursuant to 35 U.S.C. § 112 for lack of written description, and invalid pursuant to 35 U.S.C. § 103 for obviousness.

D. '251 Patent – Invalidity

Defendants allege that the asserted claims of the '251 patent are invalid pursuant to 35 U.S.C. §§ 101 & 112 for lack of utility, invalid pursuant to 35 U.S.C. § 112 for lack of enablement,

invalid pursuant to 35 U.S.C. § 112 for lack of written description, and invalid pursuant to 35 U.S.C. § 103 for obviousness.

IV. LEGAL STANDARDS

A. Infringement

Under the Patent Act "whoever without authority makes, uses, offers to sell, or sells any patented invention, within the United States or imports into the United States any patented invention during the term of the patent therefor, infringes the patent." 35 U.S.C. § 271(a). "The patentee bears the burden of proving infringement by a preponderance of the evidence." *SRI Int'l v. Matsushita Elec. Corp.*, 775 F.2d 1107, 1123 (Fed. Cir. 1985). To prove literal infringement, the patentee must show that the accused product contains every limitation in the asserted claims. *Dolly, Inc. v. Spalding & Evenflo Cos.*, 16 F.3d 394, 397 (Fed. Cir. 1994). "If even one limitation is missing or not met as claimed, there is no literal infringement." *Mas-Hamilton Grp. v. LaGard, Inc.*, 156 F.3d 1206, 1211 (Fed. Cir. 1998).

In Hatch-Waxman litigation, infringement cases are filed before the allegedly infringing product is sold. Therefore, "[t]he proper inquiry under § 271(e)(2)(A) is 'whether, if a particular drug *were* put on the market, it *would* infringe the relevant patent.'" *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1366 (Fed. Cir. 2003) (citation omitted). "[T]his hypothetical inquiry is properly grounded in the ANDA application and the extensive materials typically submitted in its support." *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1569 (Fed. Cir. 1997). "[T]he ultimate infringement inquiry . . . is focused on a comparison of the asserted patent claims against the product that is likely to be sold following ANDA approval and determined by traditional patent law principles." *Ferring B.V. v. Watson Labs., Inc.-Florida*, 764 F.3d 1401, 1408 (Fed. Cir. 2014).

B. Invalidity

Issued patents are presumed valid. *See* 35 U.S.C. § 282(a). To rebut this presumption, Defendants bear the burden of proving invalidity by clear and convincing evidence. *Titan Tire Corp. v. Case New Holland, Inc.*, 566 F.3d 1372, 1376 (Fed. Cir. 2009) ("Because of this presumption, an alleged infringer who raises invalidity as an affirmative defense has the ultimate burden of persuasion to prove invalidity by clear and convincing evidence, as well as the initial burden of going forward with evidence to support its invalidity allegation.").

i. Utility – 35 U.S.C. §§ 101 & 112

The utility requirement is established in 35 U.S.C. §§ 101 & 112.[16] A "patent may not be granted to an invention unless substantial or practical utility for the invention has been discovered and disclosed." *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1563 (Fed. Cir. 1996). It is the claims that "define the invention to be tested for utility." *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 956 (Fed. Cir. 1983). "An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip, Inc. v. Orange Bang, Inc.*, 185 F.3d 1364, 1366 (Fed. Cir. 1999). An application need only "show that an invention is useful" and "disclose a use which is not so vague as to be meaningless." *In re Fisher*, 421 F.3d 1365, 1371 (Fed. Cir. 2005). However, the utility requirement "prevents the patenting of a mere research proposal or an invention that is simply an object of research." *In re '318 Patent Infringement Litig.*, 583 F.3d 1317, 1324 (Fed. Cir. 2009).

[16] The Court notes that the American Invents Act ("AIA") amended § 112. The pre-AIA version of § 112 applies to the '663 patent, while the post-AIA version applies to the '251 patent. The relevant portion of the statute has been reformatted, but is otherwise identical in both versions.

ii. Obviousness – 35 U.S.C. § 103

To prove that an asserted claim of a patent is invalid as obvious under 35 U.S.C. § 103, Defendants bear the burden of establishing by clear and convincing evidence that the "differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious to a person having ordinary skill in the art."[17] 35 U.S.C. § 103(a). Obviousness is a question of law that is predicated on several factual inquiries. *See Richardson-Vicks v. Upjohn Co.*, 122 F.3d 1476, 1479 (Fed. Cir. 1997). Specifically, there are four considerations: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed subject matter and the prior art; and (4) secondary considerations of non-obviousness, such as long-felt but unsolved need, failure of others, praise by others in the industry, and unexpected results. *See Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966).

A party challenging the validity of a patent based on obviousness must demonstrate by clear and convincing evidence that the invention described in the patent would have been obvious to a POSA at the time the invention was made. In determining what would have been obvious to a POSA, the use of hindsight is not permitted. *See KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398, 421 (2007) (cautioning against "the distortion caused by hindsight bias" and "arguments reliant upon *ex post* reasoning"). In *KSR*, the Court acknowledged the importance of identifying "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *Id.* at 418.

"Obviousness does not require absolute predictability of success," but rather requires "a reasonable expectation of success." *See Medichem, S.A. v. Rolabo, S.L.*, 437 F.3d 1157, 1165

[17] The pre-AIA version of § 103 applies to the patents in suit.

(Fed. Cir. 2006) (quoting *In re O'Farrell*, 853 F.2d 894, 903-04 (Fed. Cir. 1988)). Obviousness "cannot be avoided simply by a showing of some degree of unpredictability in the art so long as there was a reasonable probability of success." *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1364 (Fed. Cir. 2007). While the Federal Circuit has noted that pharmaceuticals can be an "unpredictable" art to the extent that results may be unexpected, it also recognizes that evidence of a "finite number of identified, predictable solutions" or alternatives "might support an inference of obviousness." *See Eisai Co. Ltd. v. Dr. Reddy's Labs. Ltd.*, 533 F.3d 1353, 1359 (Fed. Cir. 2008) (citation omitted).

iii. Enablement – 35 U.S.C. § 112

A patent specification must contain a written description "of the manner and process of making and using [the invention], in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains . . . to make and use the same . . . ." 35 U.S.C. § 112. To be enabled, the specification must teach a POSA "how to make and use the full scope of the claimed invention without undue experimentation." *Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1378 (Fed. Cir. 2009) (citation omitted). A patentee need not "include in the specification that which is already known and available to [a POSA]" and "not every last detail is to be described, else patent specifications would turn into production specifications, which they were never intended to be." *Koito Mfg. Co. v. Turn-Key-Tech, LLC*, 381 F.3d 1142, 1156 (Fed. Cir. 2004) (citation omitted).

"Enablement is not precluded by the necessity for some experimentation such as routine screening." *In re Wands*, 858 F.2d 731, 736-37 (Fed. Cir. 1988). Furthermore, the test for undue experimentation "is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *Id.* at 737

(citation omitted). The *Wands* factors that may be considered in determining whether a disclosure would require undue experimentation include: (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims. *Id.*

iv. Written Description – 35 U.S.C. § 112

A patent's specification must "contain a written description of the invention." 35 U.S.C. § 112. The specification must "reasonably convey[] to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Ariad Pharm. Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010). The test for written description "requires an objective inquiry into the four corners of the specification from the perspective of a [POSA]." *Id.* "[W]hether a patent complies with the written description requirement will necessarily vary depending on the context. Specifically, the level of detail required . . . varies depending on the nature and scope of the claims and on the complexity and predictability of the relevant technology." *Id.* (citation omitted).

V. DISCUSSION

A. '271 Patent – Infringement

Plaintiff has asserted claim 1, the only claim, of the '271 patent. SOF ¶ 32. Claim 1 reads: "Crystalline paroxetine methanesulfonate having the following IR peaks: 531, 546, 777, 838, 931, 962, 1038, 1100, 1169, 1208, 1469, 1500, 1515, 1615, 2577, 2869, 2900, 3023." SOF ¶ 35. The Court has construed this claim to have its "[p]lain and ordinary meaning, *i.e.*, a particular form of crystalline paroxetine mesylate, which when subjected to IR spectroscopy produces a spectrum with peaks corresponding to the listed peaks." ECF Nos. 180 & 181. Plaintiff bears the burden of

showing infringement of the '271 patent by a preponderance of evidence. *Creative Compounds, LLC v. Starmark Labs.*, 651 F.3d 1303, 1314 (Fed. Cir. 2011).

As an initial matter, each of the ANDA products is crystalline paroxetine mesylate, 12/8 Tr. p.m. (Myerson) 29:16-30:20; 12/9 Tr. a.m. (Rogers) 39:20-21, and each of the ANDA products produces a spectrum when subjected to IR spectroscopy. Accordingly, the question for the Court is whether the ANDA products produce spectra with peaks corresponding to the peaks listed in the claims. Articulating its case for infringement, Plaintiff first asserts drug master file No. 028091, (the "DMF"), relied upon by Defendants in their ANDAs, contains an admission that the ANDA products "conform" to the crystalline paroxetine mesylate claimed in the '271 patent. Plaintiff next argues that there is "quite good correspondence" between the peaks in the IR spectra for the ANDA products and the claimed peaks. PFOF ¶¶ 143, 174. In quantifying the variation between the claimed values and the peaks in the spectra for the ANDA products, Plaintiff asserts that the appropriate error range is ± 14 cm^{-1} in the fingerprint region and ± 18 cm^{-1} outside the fingerprint region. In response, Defendants dispute that the DMF contains an admission of infringement. They further argue that even using the broadest error range proposed by Plaintiff, one of the claimed peaks is not present in the accused products, and accordingly, their ANDA products do not infringe. DFOF ¶ 138. Defendants also assert that a narrower error range of ± 4 cm^{-1} should be applied. DFOF ¶¶ 134-36. Infringement analysis applying an error range of ± 10 cm^{-1} was also presented to the Court. If the Court applies either of these narrower error ranges, a substantial number of claimed peaks do not have corresponding peaks in the spectra of the accused products.

DFOF ¶¶ 136-37; PFOF ¶ 143. For the reasons set forth below, the Court finds that Defendants' ANDA products do not infringe claim 1 of the '271 patent.[18]

i. The DMF does not contain an admission of infringement

In support of its infringement claim, Plaintiff first asserts that the DMF, on which both Prinston and Actavis rely, PFOF ¶¶ 89-90, contains admissions that establish the active ingredient that will be used in both ANDA products is infringing. ECF No. 227 at 3-4. Specifically, Plaintiff notes that in the section of the DMF titled "polymorphism," the DMF provides that "[a]s reported in literature, there is only one polymorphism existed [*sic*] for Paroxetine Mesylate." PTX-72.0019. The DMF concludes that the product contained in each of the batches was "determined by DSC spectrum, Infrared spectrum and X-ray and the results show that the Paroxetine Mesylate Huahai manufactured conform[s] to [the] form reported in the literature." PTX-72.0019. The DMF lists two pieces of literature considered: the '271 patent and the '927 patent, which was the other patent at issue in the Interference Proceeding. As the '271 patent is one of the listed literature references and the peaks listed in claim 1 of the '271 patent are included in the DMF, Plaintiff suggests that this constitutes an admission that the IR spectra of the ANDA products conform to the peaks claimed in the '271 patent and therefore infringe. ECF No. 227 at 3-4.

Plaintiff's suggestion does not follow from the conclusion of conformity set forth in the DMF. The DMF lists four different data sets, two sets of IR peaks, a DSC onset value and a set of XRPD peaks, providing that "[t]he detail [*sic*] information of this polymorphism is as follows:"

[18] Because there is no direct infringement, there is similarly no induced or contributory infringement.

[redacted]

PTX-72.0019. As experts for both parties agree, XRPD is a more conclusive and commonly used tool for identifying polymorphs than IR. *See* 12/8 Tr. p.m. (Myerson) 70:20-23; 12/9 Tr. a.m. (Rogers) 32:14-22. Furthermore, the DMF recognizes on its face that there is a deviation in the reported IR peak values between the '271 patent and the '927 patent, and speculates as to a possible reason for why that deviation may exist. PTX-72.0019.

The manner in which the DMF then reports the results of testing for three different batches suggests that XRPD and DSC were the controlling considerations in reaching the conclusion of conformity. The DMF reports the testing results in the following chart:

[redacted]

PTX-72.0019. [redacted]

[redacted] PTX-72.0019; *see also* 12/8 Tr. p.m. (Myerson) 75:17-78:17 (confirming that the spectra in the DMF lack all 18 peaks listed in claim 1 of the '271 patent).

In reaching its conclusion of conformity, the DMF clearly relies upon XRPD, a more definitive technique for considering polymorphs, and the XRPD values disclosed in the '927 patent. The DMF does not clearly rely on the IR values disclosed in the '271 patent. Accordingly, the Court concludes that the statement of conformity in the DMF is not an admission that the ANDA products produce IR spectra with peaks corresponding to the peaks listed in claim 1 of the '271 patent.

ii. Applying Plaintiff's preferred error range, the IR spectra of the ANDA products do not contain all of the peaks listed in claim 1 of the '271 patent

Plaintiff presented testimony from Dr. Myerson to support its claims of infringement. To assess infringement, Dr. Myerson had IR spectra generated for each Defendant's ANDA product and drew lines on the spectra at each of the wavelengths listed in the claim. 12/8 Tr. p.m. (Myerson) 45:22-53:8. Dr. Myerson performed his analysis on samples of the active ingredient described in the DMF and each Defendant's ANDA. 12/8 Tr. p.m. (Myerson) 27:20-29:5. He supervised the generation of IR spectra from Defendants' ANDA products, rather than relying on the spectra present in the ANDAs, testifying that it was better to take the data from the sample. 12/8 Tr. p.m. (Myerson) 41:9-42:2. To do so, he provided SSCI, a contract laboratory, with information about what he "wanted measured and what the protocol would be." 12/8 Tr. p.m. (Myerson) 42:4-13. Dr. Myerson had SSCI perform 64 co-added scans. 12/8 Tr. p.m. (Myerson) 60:10-15. After the spectra were generated, Dr. Myerson compared them to the peak values

claimed in the '271 patent. In doing so, he could not find a corresponding peak in the spectra for each of the claimed values. 12/8 Tr. p.m. (Myerson) 70:13-14.

As a baseline for his analysis, Dr. Myerson testified that a POSA considering the '271 patent would consider an appropriate error range to be ± 14 cm^{-1} within the fingerprint region and ± 18 cm^{-1} outside the fingerprint region.[19] 12/8 Tr. p.m. (Myerson) 22:13-23:10. Applying this error range, Dr. Myerson conceded that there is no peak in spectra that he had generated for the Prinston and Actavis samples within the error range that he set forth that corresponds to the claimed peak at 2577 cm^{-1}.[20] 12/8 Tr. p.m. (Myerson) 70:13-15. He further acknowledged that none of the spectra he considered contained all of the claimed peaks even under the broadest error range

[19] To the extent Plaintiff suggests that a POSA would not consider a particular error range or the difference between specific peaks and the claimed peaks in assessing infringement, this is undercut by the testimony of Plaintiff's own expert Dr. Myerson who expressly considered the variability of particular peaks in reaching his conclusions. *See* 12/8 Tr. p.m. (Myerson) 47:6-12 (looking at the correspondence in the fingerprint region of the Prinston spectrum and concluding that the peaks "correspond well within 10[cm^{-1}]."); *see also* PFOF ¶ 43 ("A POSA . . . would use the error range to compare the claimed peaks to the peaks in the spectrum in assessing overall correspondence.").

[20] Plaintiff's expert expressly testified that this peak was "missing" in the spectra he had generated. 12/8 Tr. p.m. (Myerson) 52:18-25. In post-trial briefing and at closing arguments, Plaintiff's counsel argued that the Court could consider peaks labeled in a spectrum in the DMF together with the peaks identified by Dr. Myerson and conclude that the peak Dr. Myerson testified was "missing" was, in fact, in the ANDA spectra. *See, e.g.*, ECF No. 236 at 4-5. In particular, Plaintiff's counsel appears to assert that it would be appropriate for the Court to find that a spot identified in the DMF spectrum at 2582 cm^{-1} corresponds to the claimed peak at 2577 cm^{-1}, and that the same peak is present in the spectra generated for Dr. Myerson's analysis. ECF No. 236 at 4-5. No testimony has been presented to suggest that the variation in the DMF spectra or the accompanying label would have been accorded any weight by a POSA. Moreover, this argument runs directly counter to the testimony of Plaintiff's own expert. The Court therefore, will not conclude that the variation in the spectra identified by Plaintiff's counsel is a "peak." In light of the lack of expert testimony on this matter, the Court will not combine the peaks from different spectra or conclude that a label identifying a spot at 2582 cm^{-1} on the spectrum in the DMF constitutes an admission that a peak is present. The labeling of that spot would require the use of a different peak-picking algorithm than was used by Plaintiff's own expert. However, Plaintiff's counsel concedes that use of a peak-picking algorithm other than the default used by their expert, Dr. Myerson, would produce a more biased result. ECF No. 236 at 4.

he considered. 12/8 Tr. p.m. (Myerson) 70:13-14, 100:3-8, 103:1-5; *see also* 12/9 Tr. a.m. (Rogers) 42:23-43:9.

Dr. Myerson suggested that this missing peak at 2577 cm^{-1} was not significant in assessing infringement because a POSA "would compare the peaks in the patent to the . . . full spectrum produced on an accused product" rather than "simply look[ing] at peak listings and try[ing] to match up peak listings." 12/8 Tr. p.m. (Myerson) 26:11-21. He further testified that in determining the appropriate weight to afford a peak, a POSA would consider the resolution at which the spectrum was measured and the intensity of the peaks at which the POSA was looking. 12/8 Tr. p.m. (Myerson) 26:22-27:4. According to Dr. Myerson, a POSA could make a determination that the spectrum had peaks corresponding to the listed peaks even if one or more peaks were missing. 12/8 Tr. p.m. (Myerson) 27:5-11. Looking at the peaks plotted on the IR spectra he had generated for each of the ANDA products, Dr. Myerson therefore concluded that "the correspondence is quite good." 12/8 Tr. p.m. (Myerson) 47:6-12, 52:18-25.

However, in construing claim 1 of the '271 patent, the Court declined to read the peaks out of the claim, but instead recognized that the listed values in the claim are subject to experimental error or a range of error. ECF Nos. 180 & 181. This is consistent with the Federal Circuit's treatment of similar claims. In *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562 (Fed. Cir. 1997), the court provided guidance on how to assess infringement of claims involving IR peaks. There, the patents in suit characterized a crystalline form "by means of a specific, 29–peak infra-red (IR) spectrum." *Id.* at 1564. Additional dependent claims also defined the crystalline form as "characterized by a 32–intensity x-ray powder diffraction pattern." *Id.* The court found that establishing one of the claimed peaks was present in the accused ANDA products was "not sufficient to substitute for the claimed 29–peak spectrum." *Id.* at 1566. The Court further

explained that "[i]t is elementary patent law that all limitations are material. The single-peak analysis was thus insufficient because, as the district court correctly noted, in order to prove infringement Glaxo was required to establish the presence of each limitation of the asserted claims." *Id.* Therefore, the Federal Circuit's analysis indicates that where a patentee claims a compound by reference to a set of IR peaks, each of those peaks constitutes an independent limitation that must be met in order to show infringement. *Id.*; *see also Cephalon, Inc. v. Sun Pharm., Ltd.*, No. 11-5474(FLW), 2012 WL 12904999, at *10-11 (D.N.J. Dec. 20, 2012) (relying on *Glaxo* and treating individual XRPD peaks as claim limitations); *Abbott Labs. v. Sandoz, Inc.*, 486 F. Supp. 2d 767, 775 (N.D. Ill. 2007) (treating individual XRPD peaks as claim limitations).

The Court rejects Plaintiff's suggestion that the finding in *Glaxo* that a single peak was not sufficient to support a finding of infringement implies that the absence of a single peak is not sufficient to defeat a claim for infringement. In any patent case, the presence of a single limitation is not sufficient to establish a claim for infringement, but the absence of a single limitation is sufficient to defeat a claim for infringement. *Glaxo, Inc.*, 110 F.3d at 1565-66 ("In order to prove infringement, a patentee must show that every limitation of the claims asserted to be infringed is found in the accused device."); *accord Seal-Flex, Inc. v. Athletic Track & Court Const.*, 172 F.3d 836, 842 (Fed. Cir. 1999) ("To show infringement of a patent, a patentee must supply sufficient evidence to prove that the accused product or process contains, either literally or under the doctrine of equivalents, every limitation of the properly construed claim."); *see also Medgraph, Inc. v. Medtronic, Inc.*, 843 F.3d 942, 949 (Fed. Cir. 2016) ("As such, a grant of summary judgment of noninfringement is proper when no reasonable factfinder could find that the accused product contains every claim limitation or its equivalent."); *Gen. Mills, Inc. v. Hunt-Wesson, Inc.*, 103 F.3d 978, 981 (Fed. Cir. 1997) ("Literal infringement requires that every limitation of the patent claim

be found in the accused infringing device."). Accordingly, the Court concludes that all of the listed peaks must be present in order to show infringement. As each Defendants' ANDA product is missing one of the claimed peaks at Plaintiff's preferred error range, Plaintiff cannot meet its burden of showing infringement.

Plaintiff suggests that this reasoning is erroneous as "[t]here is no one 'correct' set of peaks for a given spectrum, nor is it necessary to use as many as 18 peaks to characterize a spectrum," PFOF ¶ 41, implying that holding a patentee to a particular list of peaks would be improper in light of scientific realities. Logic dictates otherwise. Although there may be multiple sets of correct peaks that can be selected to characterize a spectrum, a patentee who chooses to claim a compound using a particular set of 18 peaks, for whatever reasons, should be held to that list. *Cf. Glaxo Inc. v. Novopharm Ltd.*, 931 F. Supp. 1280, 1287 (E.D.N.C. 1996), *aff'd,* 110 F.3d 1562 (Fed. Cir. 1997). Moreover, an inventor cannot include in the claim peaks that are not in the spectrum. Here, the Court notes that Plaintiff has categorically denied that there is any mistake in the peak listing. *See* 2/24 Tr. 198:10-19. Accordingly, even if the Court applies Plaintiff's preferred error range of $\pm$ 14 cm^{-1} within the fingerprint region and $\pm$ 18 cm^{-1} outside the fingerprint region, the Court finds that Plaintiff has not established infringement because each of the accused products lacks one of the claimed peaks.

iii. The error range relied upon by Plaintiff is not supported by credible testimony

The Court further notes while there is only one peak missing when Plaintiff's preferred error range of $\pm$ 14 cm^{-1} within the fingerprint region and $\pm$ 18 cm^{-1} outside the fingerprint region, is used, two other proposed error ranges were presented to the Court. Specifically, the Parties presented testimony considering infringement using error ranges of $\pm$ 10 cm^{-1} and $\pm$ 4 cm^{-1}. Under each of these error ranges, a significant number of claimed values lack corresponding peaks in the spectra of Defendants' ANDA products. For each Defendant's product, four of the eighteen

claimed peaks do not have corresponding peaks within 10 cm^{-1}, 12/8 Tr. p.m. (Myerson) 113:23-114:20, and even more claimed peaks do not have corresponding peaks within 4 cm^{-1}, *see* 12/9 Tr. a.m. (Rogers) 45:15-24; 47:23-48:11.

Furthermore, Plaintiff's own expert Dr. Myerson acknowledged under the more generous of these two ranges (± 10 cm^{-1}), a POSA could not conclude that the ANDA products were the same polymorphic form as the form claimed in the patent without further analysis. Dr. Myerson testified that while a POSA considering the peak listing in the '271 patent and the spectra of the ANDA products "would think that these *could* be the same polymorphs, they would need to do the overlay and do DSC analysis to determine they were the same form." 12/8 Tr. p.m. (Myerson) 111:2-12 (emphasis added). As explained in Section V.A.iv below, Plaintiff cannot rely on the overlay and DSC analysis to establish infringement, so if either of these more narrow error ranges is applied, Plaintiff's expert's own testimony establishes Plaintiff is unable to meet its burden of showing infringement. Because, for the reasons set forth below, the Court finds that the proposed ± 14 cm^{-1} / ± 18 cm^{-1} error range is not supported by credible testimony and a more narrow error range would apply, the Court's conclusion of non-infringement is further reinforced.

By way of background, Plaintiff relied upon the testimony of Dr. Myerson to propose an error range of ± 14 cm^{-1} / ± 18 cm^{-1}. To arrive at this range, Dr. Myerson first noted a passage in the United States Pharmacopeia ("USP"), a standard pharmaceutical reference, discussing variability in IR spectroscopy, which provides that "[t]he values may vary as much as 0.1 μm or 10 cm^{-1}, depending on the particular instrument used." 12/8 Tr. p.m. (Myerson) 4:2-18; PTX-1100.0008. He then considered the Benneker Declaration, which as discussed above described the process Dr. Benneker, one of the inventors, used to generate the peak list in claim 1. Based on Dr. Benneker's representation that he measured to the nearest 0.5 mm, Dr. Myerson concluded that

for sharp peaks the process introduced an error of approximately 4 cm^{-1}, or approximately 0.25 (half the variability introduced by Dr. Benneker's 0.5 mm approximation) multiplied by 15.38 (Dr. Benneker's scale factor). 12/8 Tr. p.m. (Myerson) 20:4-16. However, Dr. Myerson concluded that for weak, asymmetric peaks, it would be harder to determine where the peak apex is, so Dr. Benneker's technique would introduce an error of approximately 8 cm^{-1}.[21] 12/8 Tr. p.m. (Myerson) 21:23-22:8. Dr. Myerson then added these values to the 10 cm^{-1} variability described in the USP. 12/8 Tr. p.m. (Myerson) 22:9-15. Based on the location of the sharp peaks and the weak, asymmetric peaks, Dr. Myerson concluded that there would be an error range of ± 14 cm^{-1} within the fingerprint region and ± 18 cm^{-1} outside the fingerprint region. 12/8 Tr. p.m. (Myerson) 22:13-23:10.

Dr. Myerson's testimony regarding the appropriate error range has changed over the course of the litigation. Although Dr. Myerson now testifies that the appropriate error range is ± 14 cm^{-1} / ± 18 cm^{-1}, previously, he testified that the appropriate error range was 10 cm^{-1} and possibly up to 15 cm^{-1}. 12/8 Tr. p.m. (Myerson) 96:1-97:5. When he provided his earlier testimony, Dr. Myerson had already reviewed the intrinsic record of the '271 patent, including the Benneker Declaration, which he now argues supports a broader error range. 12/8 Tr. p.m. (Myerson) 96:1-97:5. Thereafter, upon reviewing the DMF, Defendants' ANDAs, and the SSCI data, which show that several peaks were outside his earlier proposed range, Dr. Myerson proposed the broader ± 14 cm^{-1} / ± 18 cm^{-1} error range. 12/8 Tr. p.m. (Myerson) 97:3-100:2. Neither Plaintiff's counsel nor Dr. Myerson has put forth a credible reason for the change in the proposed error range.

[21] Dr. Myerson's doubling of the error added by hand measuring outside the fingerprint region does not appear to derive from the intrinsic record, but instead appears to be based off of his own estimations. 12/8 Tr. p.m. (Myerson) 92:7-94:11.

Furthermore, the process Dr. Myerson used to calculate the ± 14 cm^{-1} / ± 18 cm^{-1} error range has several significant flaws. As discussed above, Dr. Myerson began his analysis by looking at the USP's discussion of variability for IR analysis and from that concluded that an appropriate baseline to start from was ± 10 cm^{-1}. 12/8 Tr. p.m. (Myerson) 92:22-93:6. In doing so, Dr. Myerson selectively read the relevant USP provision. As noted by Dr. Rogers, the USP section cited by Dr. Myerson, while not express, appears to address variation to be considered in the case of chemical identification, rather than in the case of polymorph variation. 12/9 Tr. a.m. (Rogers) 56:9-58:7; 12/9 Tr. p.m. (Rogers) 38:21-40:12. In particular, that section describes a process to avoid having polymorphism interfere with the identification of a sample by removing the existing polymorphic structure of the sample being tested and the control sample to ensure they have the same crystalline structure. PTX 1100.0008; 12/9 Tr. p.m. (Rogers) 38:21-40:12. This process would be used to determine if the two samples were the same chemical compound, but not to determine if the two samples were the same polymorph, because the process described is intended to make them the same polymorphic form. 12/9 Tr. p.m. (Rogers) 40:1-8. Moreover, independently, the USP indicates that the "values may vary *as much as* 0.1 μm or 10 cm^{-1}," PTX 1100.0008 (emphasis added), and does not indicate that a variability of greater than 10 cm^{-1} would be recognized. Because the variability among polymorphs is usually less than the variability between different chemical compounds, *see* 12/9 Tr. a.m. (Rogers) 64:22-65:2, Dr. Myerson's reliance on this section of the USP in calculating his proposed error range further undercuts his analysis.

In addition, Defendants' expert Dr. Rogers presented testimony disputing other aspects of Dr. Myerson's error range calculation. Particularly, he disputed affording special significance to the fingerprint region in the context of polymorph determination. Dr. Rogers testified that some

of the most characteristic IR peaks for polymorphs occur outside that region and that the region is primarily of importance in determining if a particular molecular structure is present in the compound.[22] 12/9 Tr. a.m. (Rogers) 49:13-22; 53:4-16 (citing DTX 191). Dr. Rogers asserted this is true in the specific case of paroxetine mesylate, as a secondary amine group in the compound absorbs IR radiation well outside the fingerprint region. 12/9 Tr. a.m. (Rogers) 50:3-24; 53:21-55:3 (citing JTX-6A). Dr. Rogers also disputed that the low resolution used by Dr. Benneker had any significant impact on the apparent location of the peaks. 12/9 Tr. a.m. (Rogers) 61:24-64:5. In short, Dr. Rogers testified persuasively that an error range of ± 14 cm^{-1} / ± 18 cm^{-1} is inappropriate.

Additionally, as a practical matter an error range of ± 14 cm^{-1} / ± 18 cm^{-1} would not allow a POSA to meaningfully assess infringement. As Dr. Myerson acknowledged, it would be unlikely that in using an error range of 18 cm^{-1} a POSA could distinguish between polymorphs from a listing of peaks. 12/8 Tr. p.m. (Myerson) 72:23-73:4. Dr. Rogers likewise testified that the error range used by Dr. Myerson was too large as it would not allow a POSA to distinguish between polymorphic forms. 12/9 Tr. a.m. (Rogers) 35:2-4. Accordingly, a more narrow error range is appropriate.

As mentioned above, when applying either of the more narrow error ranges presented to the Court (± 10 cm^{-1} and ± 4 cm^{-1}), Plaintiff cannot establish infringement. While the Court need not determine whether one of these is more appropriate, the Court notes Dr. Rogers' testimony

[22] To the extent Plaintiff argues that Dr. Rogers admitted that a POSA would not apply equal weight to low intensity peaks outside the fingerprint region, Plaintiff's argument is without merit. As Plaintiff acknowledges, the testimony at issue did not pertain to a peak resulting from paroxetine mesylate, but was instead caused by water, *i.e.*, not the compound being analyzed.

that the proper error range would be ± 4 cm^{-1},[23] 12/9 Tr. a.m. (Rogers) 35:5-7; *see also* 12/9 Tr. a.m. (Rogers) 65:3-24 (discussing JTX-037); 68:4-22 (discussing DTX-189), and Dr. Myerson's acknowledgement of the differences that a POSA would look for in distinguishing polymorphs are around 4 cm^{-1}. 12/8 Tr. p.m. (Myerson) 72:5-10.

Therefore, although Plaintiff proposes an error range of ± 14 cm^{-1} within the fingerprint region and ± 18 cm^{-1} outside the fingerprint region, under which only one peak is missing, the Court concludes that a POSA attempting to determine whether a product infringed claim 1 of the '271 patent would consider a narrower error range than ± 14 cm^{-1}.[24] The Court was also presented with infringement analysis considering an error range of ± 10 cm^{-1}, and Defendants argue that the proper error range is ± 4 cm^{-1}, under each of which a significant number of peaks are missing. Furthermore, Plaintiff's expert Dr. Myerson acknowledged that even under the broader of these two ranges, ± 10 cm^{-1}, he could not conclude that Defendants' ANDA products contained the claimed polymorph without considering DSC information and performing a spectrum overlay.

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[23] Plaintiff's counsel appears to suggest that Dr. Rogers' ± 4 cm^{-1} error range is too narrow because of the variability between identified peaks in different spectra of the same accused products. For each of the claimed peaks, Dr. Rogers identified the nearest peak in the spectra for a variety of samples. Several of these peaks differ from each other by more than 4 cm^{-1}. 12/9 Tr. p.m. (Rogers) 13:12-26:1; ECF No. 227 at 12-15. Plaintiff implies that because the nearest peaks in each spectra to the claimed peak are more than 4 cm^{-1} from each other, the error range must be more than ± 4 cm^{-1}. This reasoning is flawed. As Dr. Rogers' testimony makes clear, just because two peaks in the spectra of different samples are the closest to a claimed peak value, does not mean that they are the closest peaks to each other when all of the peaks in the sample spectra are considered. For example, for the claimed value of 531 cm^{-1} contained in the patent, in Prinston's ANDA the closest peak to the claimed value is 529.1 cm^{-1}, while the closest peak in the DMF is 539.88 cm^{-1}. While Plaintiff suggests the difference in these two values (529.1 cm^{-1} and 539.88 cm^{-1}) indicates that there must be an error range of at least 10 cm^{-1}, in reality, there is also a peak in the ANDA at 539.5 cm^{-1}, or less than 1 cm^{-1} from the value in the DMF. 12/9 Tr. p.m. (Rogers) 97:25-99:17. Accordingly, Plaintiff's argument is without merit.

[24] The experts in this case have suggested that there might be circumstances in which systemic error results in *all* the peaks being shifted in one direction or the other. That is not the case here, and the Court does not offer an opinion on how such a case should be resolved.

Because, as set forth below, Plaintiff may not rely on these additional analyses, even if the Court were to conclude that the Federal Circuit's ruling in *Glaxo* did not require every peak to be present, the Court would still conclude that Plaintiff has not met its burden of showing infringement.

iv. Plaintiff may not rely on Dr. Myerson's overlay of the ANDA spectra with the Benneker spectrum and discussion of DSC analysis to meet its burden.

Dr. Myerson performed an overlay analysis, comparing the spectra for Defendants' ANDA products to the Benneker spectrum. Performing an overlay consists of placing one spectrum on top of the other and visually assessing how they conform to each other. 12/8 Tr. p.m. (Myerson) 59:9-61:17. Overlaying the Benneker spectrum with the ANDA spectrum, Dr. Myerson concluded that they were "very, very similar spectra," although he noted that the Benneker spectrum had more noise. 12/8 Tr. p.m. (Myerson) 59:9-60:18. Dr. Myerson also noted that the DSC onset temperatures reported by Prinston and Actavis conform to the DSC onset temperature listed in the '271 patent. 12/8 Tr. p.m. (Myerson) 62:16-63:4.

The Benneker spectra and the DSC data are not in the claim at issue. It is black-letter law that the claims define the scope of a patentee's right to exclude, and therefore, to establish infringement, the accused product must be compared to the patent claims alleged to be infringed. *See Zenith Labs., Inc. v. Bristol-Myers Squibb Co.*, 19 F.3d 1418, 1423 (Fed. Cir. 1994) ("[I]t is error for a court to compare in its infringement analysis the accused product or process with the patentee's commercial embodiment or other version of the product or process; the only proper comparison is with the claims of the patent").

In the *SmithKline Beecham Corp. v. Apotex Corp.*, No. 98 C 3852, 2002 WL 1613724, at *3 (N.D. Ill. July 17, 2002), decision relied upon by Plaintiff, the district court made clear that, "the reference materials, to be an acceptable basis for a point of comparison, must exhibit each and every one of the characteristics of the hemihydrate listed in the patent." Here, there is nothing

in the record confirming that the Benneker spectrum exhibits all of the characteristics listed in the patent. Although the spectrum was in the prosecution history and was used to generate the list of peaks in the claim, the question of whether the claim actually covers the material used to generate the Benneker spectrum is at the heart of this litigation. Therefore, reliance on the Benneker spectrum's role in the generation of the claim cannot be used to circumvent the requirement of establishing that the Benneker spectrum has the claimed peaks. Plaintiff's counsel conceded that Dr. Myerson, in fact, never tried to confirm that that the Benneker spectrum actually contained all of the claimed peaks. 3/13 Tr. 147:19-22. Dr. Myerson's comparison of the Benneker spectrum to the spectra of the ANDA products does not substitute for a finding that the Benneker spectrum has all 18 peaks. Accordingly, unlike in *SmithKline Beecham Corp.*, Plaintiff has not confirmed that the reference to which it compared the accused product actually conformed to the claim. Therefore, the overlay and DSC analysis do not aid Plaintiff in satisfying its burden of establishing infringement.

v. The outcome of the Interference Proceeding does not alter the Court's analysis.

At various points, Plaintiff's counsel appear to suggest that the outcome of the Interference Proceeding supports its position that not all peaks need to be present to find infringement. *See, e.g.*, 2/24 Tr. 161:10-162:5; PFOF ¶ 35. As explained above, during the Interference Proceeding the BPAI concluded that the '743 application that gave rise to the '271 patent and SmithKline Beecham's competing '927 patent covered the same invention, even though they contained different peak listings. *See, e.g.*, ECF No. 227 at 10 n.5; PFOF ¶¶ 73-78. The Court does not afford this finding significant weight. In its claim construction opinion, the Court explained that during an interference proceeding, the interference count is considered using the broadest reasonable interpretation. *Beckmann v. Gandhi*, 646 F. App'x 950, 958 (Fed. Cir. 2016) ("Interference counts are given the broadest reasonable interpretation possible." (citation

omitted)). Under this standard, the PTO is attempting to "achieve a complete exploration of the applicant's invention." *In re Zletz*, 893 F.2d 319, 321 (Fed. Cir. 1989). In contrast, here the Court needs to look at what was actually claimed in the issued patent. *See id.* at 321-22. Accordingly, the question facing the BPAI was very different from the question this Court must answer. *See Convolve, Inc. v. Compaq Computer Corp.*, 812 F.3d 1313, 1325 (Fed. Cir. 2016) (explaining that a PTO finding under the broadest reasonable interpretation standard "cannot be dispositive" where a district court has to apply the *Phillips* standard).

Furthermore, there was evidence before the BPAI that could lead it to conclude that the "applicant's invention," as described in the '743 application was the same as what was claimed in the '927 patent without concluding that the peak listing in the '743 application was correct. Specifically, Synthon, the owner of the application, provided the BPAI with a portion of a transcript from a deposition of Dr. Benneker, one of the inventors named in the '743 application. PTX-880. In the Benneker Deposition, Dr. Benneker acknowledged that it was "correct" that the claimed value of "2577 [cm^{-1}] does not correspond to a peak.", PTX-880.0023. He further acknowledged that the claimed value of 1208 cm^{-1}, in fact, corresponded to a peak at around 1193 or 1194 cm^{-1}. Based on this, the BPAI could conclude that the underlying invention described in the '743 application was the same as the invention described in the '927 patent, even if the specific peak listings did not match. This Court is not afforded the same flexibility in considering the patent claims. *See In re Morris*, 127 F.3d 1048, 1054 (Fed. Cir. 1997) ("It would be inconsistent with the role assigned to the PTO in issuing a patent to require it to interpret claims in the same manner as judges who, post-issuance, operate under the assumption the patent is valid. The process of patent prosecution is an interactive one.").

While Synthon offered the Bennecker Deposition during the Interference Proceeding, here Plaintiff has sought to exclude it. In addition, Plaintiff asserted at trial that the peaks did not need to be corrected. 2/24 Tr. 198:13-14 ("No, your Honor, we're not asking that you correct any peaks, we're not asking that you read peaks out."). Having concluded above that these documents are not barred on timeliness or authenticity grounds, the Court must consider Plaintiff's hearsay objection. Looking at the specific contents of the Benneker Deposition, the Court concludes that it is admissible to establish how procedurally, the BPAI could have concluded that the polymorph disclosed in the '743 application was the same as the polymorph disclosed in the '927 patent despite the differences in the listed claims. *See Karol v. Burton Corp.*, 234 F. Supp. 2d 450, 457 (D. Vt. 2002). The Court does not consider the Benneker Deposition for the truth of the matter asserted therein.

Accordingly, based on the Benneker Deposition, and the differences between the rules applied for determining the scope of an invention in an interference proceeding and the rules in district court litigation, the Court concludes that the BPAI's finding that the crystalline form of paroxetine mesylate disclosed in the '743 application is the same as the form disclosed in the '927 patent is not a significant factor in determining infringement. The BPAI's decision does not alter the Court's conclusion that Plaintiff has failed to meet its burden.

B. '271 Patent – Invalidity

Although Defendants presented testimony on invalidity based on obvious-type double patenting[25] at trial, invalidity was presented in the alternative, in the event that the Court found the

[25] The judicially created doctrine of obviousness-type double patenting exists to prevent a patentee from securing a second patent on the same or obvious variation of an earlier-expiring patent claim, and thus improperly extending the right to exclude others from practicing the invention. *Abbvie Inc. v. Mathilda & Terence Kennedy Inst. of Rheumatology Tr.*, 764 F.3d 1366, 1373-74 (Fed. Cir. 2014). Obviousness-type double patenting is analyzed by first construing the two claims and then determining whether the differences between the earlier and later claim render the later-expiring

claim was infringed, *see, e.g.*, 2/24 Tr. 166:2-25. In light of the representations made to the Court that the counterclaim may be resolved, the Court will provide the Parties with an opportunity to do so.

To the extent Plaintiff argues that Defendants' non-infringement analysis is actually an invalidity argument and requires Defendants to satisfy the clear and convincing standard, Plaintiff's reliance on *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357-59 (Fed. Cir. 1999), is unavailing. That case does not mandate a shifting of burdens or relieve Plaintiff of meeting its own burden of establishing infringement in this case.

C. Method of Treatment Patents – Invalidity

Defendants challenge the validity of the method of treatment patents on a number of grounds.

i. Obviousness

Defendants first contend that the asserted claims of the method of treatment patents are invalid for obviousness under 35 U.S.C. § 103. To establish the method of treatment claims are obvious, Defendants bear the burden of proving by clear and convincing evidence that the invention of the method of treatment patents would have been obvious to a POSA in 2006 at the time of the invention. *See KSR Int'l Co.*, 550 U.S. 398; *Titan Tire Corp.*, 566 F.3d at 1376.

As discussed above, the obviousness inquiry requires analysis of four factors: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed subject matter and the prior art; and (4) secondary considerations of non-obviousness. *See Graham*, 383 U.S. at 17-18.

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claim patentably distinct from the earlier-expiring claim. *Id.* at 1374. The question of whether the claims are patentably distinct is based on a POSA's understanding as of the filing date of the later-expiring claim. *Amgen Inc. v. Hoffman-LaRoche Ltd.*, 580 F.3d 1340, 1355 (Fed. Cir. 2009).

1. The scope and content of the prior art

In analyzing obviousness, the Court must first look at the scope and content of the prior art. *See id.* The Court considers prior art regarding the use of paroxetine salts to treat vasomotor symptoms and prior art regarding paroxetine mesylate. In this case, the Court evaluates the disclosure of the two Stearns references, the Coelingh reference, and the Lemmens reference.

Stearns 2000

The first piece of prior art identified by Defendants is an article by V. Stearns, *et al.*, published in 2000 in the Annals of Oncology (JTX-33) ("Stearns 2000"). Stearns 2000 reports the results of a pilot trial assessing the efficacy of paroxetine hydrochloride in controlling hot flashes in breast cancer survivors. The study population consisted of twenty-seven women, and the study was conducted over a six-week period. For one week, the patients received 10 mg/day of paroxetine hydrochloride, and for the following four weeks, the patients received 20 mg/day of paroxetine hydrochloride. Stearns 2000 concluded that "[p]aroxetine hydrochloride is a promising new treatment for hot flashes in breast cancer survivors, and warrants further evaluation in a double-blind randomized placebo-controlled trial." JTX-33 at NOV-BRIS-0167591. It further stated "the data from this pilot trial strongly suggest that paroxetine hydrochloride is an effective therapy for hot flashes in breast cancer survivors." JTX-33 at NOV-BRIS-0167595. Stearns 2000 was before the Patent Office during the prosecution of the method of treatment patents.

Stearns 2005

Defendants also cite the published report of a follow up study to Stearns 2000. In 2005, Stearns, *et al.*, published the results of a much larger, randomized clinical trial testing the efficacy of paroxetine in treating hot flashes in the Journal of Clinical Oncology, (JTX-034) ("Stearns 2005"). The study reported in Stearns 2005 was designed as a crossover study, with each patient either receiving 10 mg/day of paroxetine or 20 mg/day of paroxetine during the treatment period.

The authors concluded that the 10 mg/day treatment and the 20 mg/day treatment "were similar in effectiveness for reducing hot flash frequency and composite scores." JTX-34 at ACTBRIS0013957. The authors also noted that the toxicity profile of the 10 mg/day dose was more favorable than the 20 mg/day dose, and accordingly the authors "recommend[ed] prescribing [a] low-dose of paroxetine (10 mg) to women who desire a nonhormonal pharmacologic treatment for their hot flashes." JTX-34 at ACTBRIS0013962. Stearns 2005 was before the Patent Office during the prosecution of the method of treatment patents.

Coelingh

The third piece of prior art relied upon by Defendants is an international patent application published in 2002, (PTX-0982) ("Coelingh"). Coelingh describes a method of treating hot flashes by administering a combination of serotonin re-uptake inhibitor and vitamin B6.[26] PTX-982.0002; 12/12 Tr. p.m. (Locker) 60:24-61:12. Coelingh identifies twelve preferred serotonin re-uptake inhibitors and further lists nine of those twelve, including paroxetine, as the most preferable. PTX-982.0010; 12/14 Tr. (Simon) 90:5-91:4. Coelingh does not further single out paroxetine from that list of nine. 12/12 Tr. p.m. (Locker) 68:1-5; 12/14 Tr. (Simon) 9:20-23.

While Coelingh only directly provides dose amounts for trazodone, another serotonin re-uptake inhibitor, it provides "conversion factors" to convert the listed doses of trazodone into dose amounts for the other most preferable compounds. PTX-982.0010. It does not indicate how the different conversion factors were determined. *See* 12/12 Tr. p.m. (Locker) 71:7-72:1; 12/14 Tr. (Simon) 8:24-9:3; *see also* 12/14 Tr. (Woodworth) 130:11-14.

[26] Although Coelingh discloses co-treatment with vitamin B6, the claims of the patents in suit are open claims that would encompass co-treatment.

Applying the conversion factor for paroxetine to claim 2 of the Coleingh reference, Defendants' expert Dr. Locker calculated that the dose range for paroxetine would be between 0.09 mg/day and 12 mg/day. 12/12 Tr. a.m. (Locker) 107:8-108:8. Applying the conversion factor to the most preferable embodiment described in the application, and using the mean weight of a woman in her fifties, Dr. Locker calculated that the dose range for paroxetine would be between 0.21 mg/day and 8.4 mg/day. 12/12 Tr. a.m. (Locker) 107:8-109:20. While the range would obviously vary based on the actual weight of a patient, *see* 12/14 Tr. (Simon) 11:23-12:4, Dr. Locker's use of the mean weight of 70 kg was reasonable. It is the average weight of a women between 50 and 59, 12/14 Tr. (Simon) 89:7-17; DTX 361, and the values Dr. Locker calculated using the 70 kg average weight are consistent with the values that he calculated using the conversion factor and the dose range disclosed in claim 2.

Admittedly, the only example provided in Coelingh is for fluoxetine rather than paroxetine and appears to be prophetic, as it does not describe a study that was actually performed. 12/12 Tr. p.m. (Locker) 38:18-42:6. Coelingh was not before the Patent Office during the prosecution of the method of treatment patents.

Lemmens

The final significant piece of prior art relied upon by Defendants is a 2004 U.S. patent application. (PTX-983) ("Lemmens"). In Lemmens, the applicant discussed the advantages of paroxetine mesylate over paroxetine hydrochloride for pharmaceutical use, noting its better thermal stability.

2. *The Level of Ordinary Skill in the Art*

The Parties dispute the level of ordinary skill in the art of the '663 and '251 patents. Plaintiff asserts that a POSA would have an M.D. and at least five years of experience in the treatment of vasomotor symptoms, such as a gynecologist, general internist, family practitioner,

or oncologist. PFOF ¶ 206. Defendants assert that a POSA would have at least a Bachelor's degree and most likely a medical degree, and would have some experience treating women with thermoregulatory dysfunction. DFOF ¶ 35; 12/12 a.m. (Locker) 110:13-17. Defendants' expert Dr. Locker, however, indicates that a POSA, in fact, would have a medical degree. 12/12 a.m. (Locker) 111:6-9, 112:5-9. The Court considers the testimony presented and the nature of the patents, which are directed to methods of treating patients with vasomotor symptoms, something that would presumably be done by a medical doctor with experience doing so. Accordingly, the Court concludes that a POSA would have a medical degree and experience treating vasomotor symptoms.

Plaintiff further suggests that a POSA would have, or would work with someone who had, a Ph.D. in pharmacy, pharmaceutical sciences, or pharmacology, with a focus on pharmacokinetics or pharmacodynamics and at least five years of experience. PFOF ¶ 206; 12/13 Tr. (Simon) 139:10-141:6. Defendants claim that a POSA would not need to have a Ph.D. in pharmacokinetics or pharmacodynamics. DFOF ¶ 36; 12/12 a.m. (Locker) 111:19-112:1. The method of treatment patents do not contain reference to pharmacokinetic or pharmacodymic data or theories. Accordingly, the Court finds that while a POSA might have exposure to pharmaceutical sciences or pharmacology, a POSA would not necessarily have a Ph.D. or any significant experience in those fields. *See Daiichi Sankyo Co. v. Apotex, Inc.*, 501 F.3d 1254, 1257 (Fed. Cir. 2007) (considering the types of testing disclosed in the specification when assessing the level of skill in the art).

3. The Differences Between the Claimed Subject Matter and the Prior Art

Plaintiff asserts claims 1, 2, and 5 of the '663 patent, SOF ¶ 41, and claims 1, 2, 4, 9, and 10 of the '251 patent. SOF ¶ 55.

Claim 1 of the '663 patent claims:

> 1. A method for treating a patient suffering from a thermoregulatory dysfunction associated with menopause comprising administering paroxetine mesylate to said patient in an amount, based on the paroxetine moiety,[27] of 7.5 mg/day.

Claim 2 of the '663 patent is dependent on claim 1, and claims:

> 2. The method of claim 1, wherein said thermoregulatory dysfunction is a condition selected from the group consisting of hot flashes, hot flushes, night sweats and combinations thereof.

Claim 5 of the '663 patent claims:

> 5. A method for treating a patient suffering from a thermoregulatory dysfunction associated with menopause comprising administering paroxetine to said patient, wherein said paroxetine is in the form of a pharmaceutically acceptable mesylate salt, in amorphous or crystalline form, and mixtures thereof, wherein said paroxetine mesylate is administered in an amount, based on the paroxetine moiety, of 7.5 mg/day.

Claim 1 of the '251 patent claims:

> 1. A method for treating a patient suffering from a thermoregulatory dysfunction associated with menopause, comprising administering a dosage form of paroxetine to said patient in an amount, based on the paroxetine moiety, of 7.5 mg/day.

Claim 2, 4, 9, and 10 of the '251 patent are dependent on claim 1, and claim:

> 2. The method of claim 1, wherein said thermoregulatory dysfunction is a condition selected from the group consisting of hot flashes, hot flushes, night sweats and combinations thereof.
>
> 4. The method of claim 1, wherein the dosage form comprises a pharmaceutically acceptable salt of paroxetine.
>
> 9. The method of claim 1, wherein the dosage form comprises paroxetine or a pharmaceutically acceptable salt thereof in anhydrate, hydrate, or solvate form, or combination of two or more thereof.

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[27] The paroxetine moiety is the paroxetine molecule without the salt component. 12/12 Tr. a.m. (Meyerson) 17:11-16. The mass of the paroxetine moiety can be obtained from the mass of the salt by comparing the molecular weight of the moiety to the molecular weight of the salt. 12/12 Tr. a.m. (Meyerson) 18:5-21.

> 10. The method of claim 1, wherein the dosage form comprises paroxetine or a pharmaceutically acceptable salt thereof in a crystalline or amorphous form, or a combination thereof.

Collectively, the four prior art references presented disclose all of the limitations of the asserted claims except the particular value of 7.5 mg/day, which falls within the range disclosed in Coelingh. Stearns 2005 established that 10 mg/day doses of paroxetine hydrochloride were effective for treating hot flashes. Using the conversion factor contained within, Coelingh discloses the treatment of hot flashes with between 0.09 mg/day and 12 mg/day of paroxetine. Plaintiff challenges this disclosure and suggests that a POSA would view it as incredible. However, prior art is presumptively enabled, *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1354 (Fed. Cir. 2003), and Plaintiff has not rebutted that presumption here. Finally, Lemmens discloses that paroxetine mesylate is preferable to paroxetine hydrochloride. Because the prior art brings together all of the elements of the asserted claims except the precise value of 7.5 mg/day, which is within the range in Coelingh, the differences between the claimed subject matter and the prior art are minimal. Although this does not end the Court's analysis, as set forth below, it strongly indicates that the claimed inventions are obvious.

4. Secondary Considerations of Non-Obviousness

"An obviousness analysis requires a Court to also examine objective evidence of nonobviousness in the record." *Janssen Pharmaceutica N.V. v. Mylan Pharm., Inc.*, 456 F. Supp. 2d 644, 669 (D.N.J. 2006) (citations omitted). "Objective evidence of nonobviousness can include copying, long felt but unsolved need, failure of others, commercial success, unexpected results created by the claimed invention, unexpected properties of the claimed invention, licenses showing industry respect for the invention, and skepticism of skilled artisans before the invention." *Power Integrations, Inc. v. Fairchild Semiconductor Int'l, Inc.*, 711 F.3d 1348, 1368 (Fed. Cir. 2013). For evidence of a secondary consideration to be relevant, there must be a nexus between the

evidence and the claimed invention. *See Ormco Corp. v. Align Tech., Inc.*, 463 F.3d 1299, 1311-12 (Fed. Cir. 2006); *AstraZeneca LP v. Breath Ltd.*, 88 F. Supp. 3d 326, 387 (D.N.J. 2015), *aff'd*, 603 F. App'x 999 (Fed. Cir. 2015). Plaintiff asserts (1) Brisdelle satisfied a long-felt but unmet need for a non-hormonal vasomotor treatment, (2) there was a long history of failure of others to develop a safe and effective non-hormonal treatment for vasomotor symptoms, (3) there was industry recognition of Brisdelle, and (4) there were unexpected results associated with use of 7.5 mg/day paroxetine for treating vasomotor symptoms.

Long-felt Need

"Evidence of a long felt but unresolved need tends to show non-obviousness because it is reasonable to infer that the need would have not persisted had the solution been obvious." *WBIP, LLC v. Kohler Co.*, 829 F.3d 1317, 1332 (Fed. Cir. 2016). "If prior art products were effective for the purpose of the claimed invention, there is no long-felt need." *AstraZeneca LP*, 88 F. Supp. 3d at 387. "Evidence of the long-felt need factor must squarely address the need satisfied by the asserted claims themselves." *Id.* Plaintiff argues that Brisdelle satisfied a long-felt but unmet need for a non-hormonal treatment for vasomotor symptoms, PFOF ¶ 351, because at the time of the invention, the only FDA-approved therapy to treat vasomotor symptoms was hormonal therapy, PFOF ¶ 350.

There is substantial evidence that non-hormonal, prior art products were effective for treating vasomotor symptoms, so there was no unmet need. As set forth above, by 2005, doctors were prescribing 10 mg doses of Paxil off-label for treatment of hot flashes, 12/12 Tr. a.m. (Locker) 98:19-99:7, and doctors were using other SSRIs and SNRIs to treat hot flashes.[28] 12/12

[28] Although these products were not FDA approved for that purpose, and the FDA subsequently stated that there was an "unmet need for an FDA-approved non-hormonal treatment option for vasomotor symptoms," PTX-626.0004, it is clear that by the time of the invention, doctors were prescribing a wide-array of different non-hormonal products for the treatment of vasomotor

Tr. a.m. (Locker) 97:15-20. Moreover, even after FDA approval was granted for Brisdelle, doctors continued to overwhelmingly prescribe other products off-label, further affirming the Court's conclusion that other products were on the market that met the claimed need.[29] As Plaintiff's Chief Commercial Officer Mr. Briggs testified "Brisdelle meets an unmet need as a viable *choice* for patients, and women, and doctors," 12/13 Tr. (Briggs) 23:8-12 (emphasis added), suggesting that Brisdelle was merely an addition to an already existing market in which patients had other choices they could turn to in order to meet their needs. Additionally, Mr. Briggs testified that many patients may not find their vasomotor symptoms "bothersome enough" to justify taking a drug, 12/13 Tr. (Briggs) 24:7-13, further suggesting that there was not a significant need for the invention.

Even if the Court assumed Brisdelle met a need, this need was not "long-felt." The safety concerns motivating the need for a non-hormonal treatment "gained attention in 2002 with the Women's Health Initiative (WHI) study, which found significant risks associated with [hormone replacement therapy]." PFOF ¶ 348. This was only around four years before the filing date of the

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symptoms. *Avanir Pharm., Inc. v. Actavis S. Atl. LLC*, 36 F. Supp. 3d 475, 508 (D. Del. 2014) (finding no long-felt need where the off-label use of other drugs was considered by the medical community to be safe and effective at treating the targeted condition), *aff'd per curiam sub nom. Avanir Pharm. Inc. v. Par Pharm. Inc.*, 612 F. App'x 613 (Fed. Cir. 2015); *see also AstraZeneca LP v. Breath Ltd.*, 88 F. Supp. 3d at 388 (finding there was no long-felt need where a prior art drug met the need even though the prior art drug was not available for sale in the United States as it was not approved by the FDA).

[29] The Court notes that the Parties dispute the relevance of Brisdelle's lack of acceptance in the marketplace as established by its market performance. It is clear that Brisdelle substantially underperformed market forecasts and has not achieved widespread adoption, as even under Plaintiff's most favorable calculations, by May 2014, Brisdelle only constituted [redacted] of the *non-hormonal* treatments prescribed by those doctors Noven was *targeting* with its sales. PTX-0457-0060; 12/13 (Jarosz) 107:12-24; *see also* 12/13 Tr. (Briggs) 23:2-12, 26:7-27:12, 30:7-15, 47:8-17; 12/14 Tr. (Hofmann) 171:14-17, 173:20-174:9. Failure in the marketplace may indirectly suggest that a product did not meet a long-felt but unmet need as patients and doctors turn to other treatment options or choose to forego treatment altogether. *See* 12/13 Tr. (Briggs) 24:7-13. However, the Court need not consider this evidence to arrive at its conclusion that the invention of the method of treatment patents did not satisfy a long-felt but unmet need.

'586 application that ultimately gave rise to the method of treatment patents, indicating that the need was not long-felt. *See Purdue Pharm. Prod. L.P. v. Actavis Elizabeth LLC*, No. CIV.A. 12-5311 JLL, 2015 WL 5032650, at *49 (D.N.J. Aug. 25, 2015) (stating that the four years between the prior art clearly articulating the need and the preparation of the patented product was "hardly 'long-felt'"). Accordingly, the Court finds that the claimed inventions did not meet an unmet need and even if such a need existed, it was not long-felt.

Failure of Others

Although the claimed invention of the method of treatment patents did not satisfy a long-felt need, Brisdelle is the only FDA approved non-hormonal option to treat vasomotor symptoms. 12/13 Tr. (Briggs) 21:11-12. Two other drugs were submitted to the FDA for approval as non-hormonal treatments for vasomotor symptoms, desvenlafaxine and gabapentin, neither of which gained approval. PFOF ¶ 378; 12/14 Tr. (Simon) 19:5-21:15, 21:19-24:6. Failure to obtain FDA approval is a benchmark in evaluating failure of others. *Pfizer Inc. v. Teva Pharm. USA, Inc.*, 460 F. Supp. 2d 659, 662 (D.N.J. 2006). Accordingly, the Court concludes the failure of others weighs against Defendants' claim of obviousness.

Industry Recognition

Plaintiff also suggests that industry recognition supports a finding of non-obviousness. Much of the evidence cited by Plaintiff merely represents the uncontroversial acknowledgement by industry (including a consultant for Noven), that the FDA approved Brisdelle. *See* PTX-942, PTX-945, PTX-1052; PFOF ¶¶ 361-65. The remainder of Plaintiff's references suggest at best a muted response to Brisdelle. *See, e.g.*, PTX-1052.0008 ("[Brisdelle] does not provide any unique pharmacological advantage over low-dose paroxetine HCl which may also be administered at bed-time to reduce adverse effects."). Accordingly, the Court concludes that Plaintiff's position of non-obviousness is not supported by industry recognition.

Unexpected results

"Unexpected results that are probative of nonobviousness are those that are 'different in kind and not merely in degree from the results of the prior art.'" *Galderma Labs., L.P. v. Tolmar, Inc.*, 737 F.3d 731, 739 (Fed. Cir. 2013) (quoting *Iron Grip Barbell Co. v. USA Sports*, 392 F.3d 1317, 1322 (Fed. Cir. 2004)). "To be particularly probative, evidence of unexpected results must establish that there is a difference between the results obtained and those of the closest prior art." *Bristol-Myers Squibb Co. v. Teva Pharm. USA, Inc.*, 752 F.3d 967, 977 (Fed. Cir. 2014). Later-discovered differences can support a finding of unexpected results. *Genetics Inst., LLC v. Novartis Vaccines & Diagnostics, Inc.*, 655 F.3d 1291, 1307 (Fed. Cir. 2011).

Plaintiff argues that the invention of the method of treatment patents displayed unexpected results. In particular, Plaintiff notes that while the use of paroxetine at higher doses to treat depression is associated with weight gain, sexual dysfunction and severe discontinuation symptoms, PFOF ¶ 367, Phase III studies showed that treatment with 7.5 mg/day of paroxetine was "not associated with weight gain or change in sexual function in women with moderate to severe [vasomotor symptoms] with menopause." PFOF ¶ 369 (quoting PTX-1032.7). Similarly, the Phase III studies also showed a lack of discontinuation symptoms. PFOF ¶¶ 372-73. However, as set forth above, Stearns 2005 suggested that there was a dose relationship for side effects between 20 mg/day and 10 mg/day, PFOF ¶ 296, and over the course of the study while there was a low instance of side effects at 10 mg/day, they were not statistically significant, PFOF ¶¶ 297, 299; 12/14 Tr. (Simon) 6:16-19. Therefore, a POSA considering the Stearns 2005 study would reasonably expect that side effects would decrease as doses decreased, particularly in light of the general understanding that if you lower the dose of a drug, side effects decrease. *See* 12/14 Tr. (Simon) 86:10-25; DTX-194; *cf.* 12/12 Tr. a.m. (Locker) 100:18-101:7; *Galderma Labs., L.P.*, 737 F.3d at 739 ("In this case, the expected result was an increase, by some percentage, in the

prevalence of certain side effects. The failure of that percent increase to materialize, though unexpected, constitutes only a difference in degree from the prior art results."). Accordingly, the claimed invention does not demonstrate unexpected results.[30]

5. Claim 1 of the '271 Patent is Obvious in Light of the Prior Art

As discussed above, the obviousness inquiry requires analysis of four factors: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed subject matter and the prior art; and (4) secondary considerations of non-obviousness. *See Graham*, 383 U.S. at 17-18. The Supreme Court has also instructed that "[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR Int'l Co.*, 550 U.S. at 416. In assessing obviousness, "it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *Id.* at 418. As explained below, after analyzing the relevant factors, the Court concludes that the asserted claims of the method of treatment patents are invalid as obvious.

The method of treatment patents claim the use of 7.5 mg/day of paroxetine mesylate (or another form of paroxetine) to treat vasomotor symptoms. Stearns 2005 demonstrated that 10 mg/day of paroxetine hydrochloride was effective to treat vasomotor symptoms. Coelingh disclosed treatment of vasomotor symptoms with between 0.09 mg/day and 12 mg/day of paroxetine, or most preferably, with between 0.21 mg/day and 8.4 mg/day. Lemmens disclosed that paroxetine mesylate is preferable to paroxetine hydrochloride. In short, the only element not

[30] As set forth below, a POSA would likewise not consider the continued efficacy at a lower dose to be unexpected.

expressly disclosed in the prior art is the specific dose of 7.5 mg/day, which falls within the ranges disclosed in Coelingh.

The 7.5 mg/day value is not a critical value in the method of treatment patents. The Federal Circuit has held that the disclosure of a broad range of doses in the specification indicates that the particular value claimed is not "critical" absent explanation. *Warner Chilcott Co., LLC v. Teva Pharm USA, Inc.*, 642 F. App'x 996, 1002 (Fed. Cir. 2016). Here, the specifications state efficacy at doses from 0.1 mg/day to 10 mg/day, and nothing in the patent otherwise identifies the particular dose claimed (7.5 mg/day) as significant. In fact, 7.5 mg/day dosing is not included in either example provided in the specification. DFOF ¶ 17. Instead, the claims were narrowed to 7.5 mg/day during prosecution after the completion of Phase II trials testing efficacy, which used a 7.5 mg/day dose. JTX-9 at NOV-BRIS-0167101; *see also* 12/12 Tr. p.m. (Locker) 7:17-24, 50:3-6; 12/14 Tr. (Simon) 37:25-38:24. Furthermore, the named inventor's own testimony indicates someone else selected 7.5 mg/day value for the claims after the filing of the initial patent application. Richards Dep. 60:25-61:12, 89:22-90:1. When asked how she arrived at the value of 7.5 mg/day, Dr. Richards testified that she thought there was an "initial proposal . . . to study [redacted]' in clinical trials, but she could not testify as to what was actually done in the clinical trials because she was no longer involved with the project. Richards Dep. 60:25-61:12; *see also* Richards Dep. 89:22-90:1 ("Well, the other thing is 7.5 milligrams per day, that was put in later. So, you know, I can't answer that. That wasn't in the original patent, specifically, that dose."). Accordingly, in light of the broad disclosure and the range disclosed in the prior art, the specific recitation of 7.5 mg/day in the claims does not provide substantial support for a finding of non-obviousness. *See ClearValue, Inc. v. Pearl River Polymers, Inc.*, 668 F.3d 1340, 1345 (Fed. Cir. 2012) (holding that while the disclosure of a broad genus does not disclose every species within

that genus, where there is "no allegation of criticality or any evidence demonstrating any difference across the range" the disclosure of the range in the prior art discloses the value within the range).

Given that the 7.5 mg/day value claimed is not critical, the range disclosed in Coelingh teaches this value. As set forth above, Coelingh expressly contemplates treatment with doses of less than 10 mg/day and with a range that includes 7.5 mg/day. The Federal Circuit stated in *Iron Grip Barbell Co. v. USA Sports, Inc.*, that "where there is a range disclosed in the prior art, and the claimed invention falls within that range, there is a presumption of obviousness." 392 F.3d at 1322. The Federal Circuit subsequently clarified, that "all evidence relevant to obviousness or nonobviousness must be considered, and be considered collectively." *In re Cyclobenzaprine Hydrochloride Extended-Release Patent Litig.*, 676 F.3d 1063, 1078 (Fed. Cir. 2012). Courts have continued to treat *Iron Grip* as instructive while being sure to consider all relevant evidence collectively. *See, e.g., Warner Chilcott Co., LLC v. Teva Pharm. USA, Inc.*, 89 F. Supp. 3d 641, 673 (D.N.J. 2015), *aff'd,* 642 F. App'x 996 (Fed. Cir. 2016); *AstraZeneca LP*, 88 F. Supp. 3d at 378. While Plaintiff asserts that in *Iron Grip* the range disclosed in the prior art was more limited than the range here, a dosage range of 10 mg/day is still quite narrow, and in *Tyco Healthcare Grp. LP v. Mut. Pharm. Co.*, 642 F.3d 1370, 1373 (Fed. Cir. 2011), the court considered *Iron Grip* and found that prior art disclosing a dosage range of 5 to 15 mg rendered obvious a claimed dose of 7.5 mg. Here, the Court is faced with an almost identical range, and concludes that Coelingh's disclosure of the most preferable range of 0.21 mg/day to 8.4 mg/day is strong evidence that the claimed value of 7.5 mg/day is obvious.

In addition to simply disclosing this range, the prior art would motivate a POSA to use a lower than 10 mg/day dose of paroxetine, such as 7.5 mg/day, to treat vasomotor symptoms. Stearns 2005 suggested that there was no dose relationship for efficacy between 20 mg/day and 10

mg/day,[31] PFOF ¶ 295, so decreasing the dose of paroxetine did not decrease its effectiveness at reducing hot flashes. Stearns 2005 also suggested that there was a dose relationship for side effects between 20 mg/day and 10 mg/day, PFOF ¶ 296, so decreasing the dose of paroxetine did result in a decrease in side effects. While Plaintiff suggests that there would be no incentive to decrease the dose further from 10 mg/day because Stearns 2005 did not report significant side effects with 10 mg/day relative to placebo, there was still a "low incidence of side effects with 10 mg/day," PFOF ¶¶ 297, 299. More significantly, the treatment period in Stearns 2005 was only 4 weeks, JTX-034, and it was known that the weight gain side effect of paroxetine manifested "over long-term use after 6 months," PFOF ¶ 285; *accord* DFOF ¶ 216. Therefore, a POSA would be motivated to use doses lower than 10 mg/day in order to further reduce side effects, with a reasonable belief that efficacy would not be significantly affected. It is, therefore, clear that all of the elements of the claims were present in the prior art, and there was a motivation to combine them.

Finally, as the above discussion makes clear, contrary to Plaintiff's position, a POSA would have been motivated to select paroxetine to treat vasomotor symptoms. Stearns 2005 expressly recommends the use of paroxetine to treat vasomotor symptoms. JTX-34. Doctors, in fact, followed this recommendation and prescribed 10 mg/day of paroxetine to treat patients with hot flashes. 12/12 a.m. Tr. (Locker) 98:19-21. Although paroxetine had various side effects, Stearns 2005 established that short-term side effects were not statistically significant at lower doses.

[31] Although Plaintiff presented testimony that paroxetine exhibits non-linear pharmacokinetics, 12/14 Tr. (Woodworth) 121:3-13, and non-linear pharmacokinetics can make dosing unpredictable, 12/14 Tr. (Woodworth) 124:15-19, nothing in the patent refers to pharmacokinetic or pharmacodynamics information, and Plaintiff's Investigational New Drug Application informed the FDA that [redacted]. 12/14 Tr. (Woodworth) 136:12-137:25. Accordingly, the Court does not find this testimony persuasive.

Plaintiff also suggests that a POSA would not choose paroxetine because paroxetine was known to interfere with the efficacy of tamoxifen, a common treatment for breast cancer patients, a population that would benefit from a non-hormonal treatment. PFOF ¶ 287. However, there is still a significant population that may desire a non-hormonal option but that is not receiving treatment with tamoxifen. For example, the Court notes that the Stearns 2000 study considered the population of breast cancer survivors.

Stearns 2000 and Stearns 2005 established that the active ingredient paroxetine was effective for treating hot flashes at doses as low as 10 mg/day. Coelingh disclosed that a dose of 0.09 mg/day to 12 mg/day could be used for treating hot flashes. Lemmens made clear that of the paroxetine salts currently in use, paroxetine mesylate has significant advantages in terms of pharmaceutical stability. Given the dose relationship observed for side effects, and the lack of a similar relationship for efficacy, a POSA would be motivated to use doses of less than 10 mg/day and would have a reasonable expectation that they would work. As discussed above, while there was a failure of others, the claimed invention did not satisfy a long-felt need and there was not unexpected benefits or industry recognition. Accordingly, the Court concludes that the asserted claims of the '663 and '251 patents are invalid as obvious under 35 U.S.C. § 103.

ii. Utility

Defendants allege that if the asserted claims of the method of treatment patents are not invalid as obvious, they are invalid for failure to meet the utility requirement of 35 U.S.C. § 101 and through it, the enablement requirement of § 112. *In re Ziegler*, 992 F.2d 1197, 1200 (Fed. Cir. 1993) ("The how to use prong of section 112 incorporates as a matter of law the requirement of 35 U.S.C. § 101 that the specification disclose as a matter of fact a practical utility for the invention."). To prove that the method of treatment patents lack utility, Defendants bear the burden of demonstrating by clear and convincing evidence that the disclosure does not provide adequate

evidence that a POSA would view the disclosed utility as credible. *See In re '318 Patent Infringement Litig.*, 583 F.3d 1317, 1327 (Fed. Cir. 2009); *Titan Tire Corp.*, 566 F.3d at 1376.

Defendants contend that if the method of treatment claims are not found to be obvious, then additional test data would have been required to establish credible utility. Plaintiff argues that while the prior art does not render the method of treatment patents obvious, the method of treatment patents read in light of the prior art establish credible utility. Plaintiff further argues that in assessing utility the Court may properly consider a September 13, 2010 declaration submitted by Dr. Joel Lippman, the Chief Medical Officer of Noven, during the prosecution of the method of treatment patents, (JTX-9 at NOV-BRIS-167094) (the "Lippman Declaration"), which described the results of a clinical trial establishing that 7.5 mg/day of paroxetine mesylate is effective for treating vasomotor symptoms. Defendants assert that consideration of this post-filing submission is improper.

As discussed above, the Court found that the method of treatment patents are invalid as obvious. However, if the Court had found the method of treatment patents nonobvious, the Court would have concluded that the asserted claims are invalid for lack of credible utility.[32] Plaintiff's experts' own testimony would by itself establish to a clear and convincing standard, that the patent lacked credible utility given the *de minimis* nature of the disclosure made by the patentee, which did not contain any test data, animal model descriptions, in vitro data, or explanation of the mechanism of action of the drug. *See* 12/12 Tr. p.m. (Locker) 10:12-11:3.

Utility is assessed as of the application filing date. *In re Brana*, 51 F.3d 1560, 1567 n.19 (Fed. Cir. 1995). As filed, the applications giving rise to the method of treatment patents set forth

[32] By this, the Court does not intend to suggest that it views this matter as a dichotomy in which the patent is either invalid as obvious or invalid for lack of utility, as among other things in considering utility, unlike obviousness, a POSA would consider the disclosure made by the patent.

a range of doses claimed to be effective. The specifications did not provide any support for the doses set forth therein other than what is in the prior art. There are no additional clinical studies described, no animal studies, and no further elucidation of the mechanism of action. Although there were two prophetic examples in the specifications, it was clear that several of the doses included in those specifications would not likely be effective as described. As Dr. Richards, the sole inventor named in the method of treatment patents acknowledged, a POSA would not believe that dosing at the lower end of the range disclosed was likely to be effective and these doses were added to the specifications after consultation with a patent attorney. Richards Dep. 78:11-79:3, 80:1-9; 81:12-22.

Thus, all the method of treatment patents add to the prior art is the identification of 7.5 mg/day in the claims, without any justification for this value. Plaintiff's expert Dr. Simon acknowledged that more data would be needed to establish that 7.5 mg/day of paroxetine mesylate would be effective to treat hot flashes. Dr. Simon appears to have testified during his deposition that it was reasonable to expect that 7.5 mg/day of paroxetine mesylate would work to treat hot flashes based on the prior art without the benefit of the Phase II data, 12/14 Tr. (Simon) 74:19-23. However, at trial, he testified "[w]ithout the benefit of the Phase II data, I think you'd have to test it." 12/14 Tr. (Simon) 72:12-16; 12/14 Tr. (Simon) 99:7-100:4.[33]

That testing came later during the prosecution and was reported in the Lippmann Declaration. The Lippmann declaration reported the results of a Phase II clinical trial, which showed that 7.5 mg/day was effective for the treatment of hot flashes. 12/12 Tr. p.m. (Locker) 50:3-6. Following the submission of the Lippmann Declaration, the claims were narrowed to a

[33] The Court notes that while Plaintiff attempted to restrict Dr. Woodworth's testimony to the issue of obviousness, *see* 12/14 Tr. (Woodworth) 162:12-20, the opinions he expressed are consistent with Dr. Simon's testimony. *See, e.g.*, 12/14 Tr. (Woodworth) 153:5-13, 160:5-8, 160:22-23.

dose of 7.5 mg/day. 12/12 Tr. p.m. (Locker) 7:10-24; 12/14 Tr. (Simon) 37:25-38:24. Plaintiff asserts that it may rely on the Lippmann Declaration to establish utility in light of the Federal Circuit's decision in *In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995). However, the Lippmann declaration is not being used in the same manner as the post-filing data in *In re Brana*. In *Brana*, the court found that a POSA "would be without basis to reasonably doubt applicants' asserted utility on its face." *Id.* at 1566.[34] The court in dicta merely noted the permissibility of relying on a declaration dated after the filing date "to substantiate any doubts as to the asserted utility since [the declaration] pertains to the accuracy of a statement already in the specification." *Id.* at 1569 n.19. Here, by contrast, based on the testimony of Plaintiff's own experts, there is no specific statement in the specification to which a subsequent declaration could be used for amplification. Rather, a POSA would have a basis to reasonably doubt the applicant's asserted utility on its face, particularly since there is nothing in the specification distinguishing between extremely low doses, doubted by the witnesses, and the 7.5 mg/day dose that was ultimately claimed.

The Court must be careful not to let the "narrow exception to the rule that post-filing data cannot support utility" articulated in *Brana* "swallow the rule that '[e]nablement, or utility, is determined as of the application filing date.'" *CreAgri, Inc. v. Pinnaclife, Inc.*, No. 11-CV-6635-LHK, 2013 WL 6673676, at *19 (N.D. Cal. Dec. 18, 2013) (quoting *In re Brana*, 51 F.3d at 1567 n.19), *aff'd*, 579 F. App'x 1003 (Fed. Cir. 2014). While post-filing data may be able to substantiate predicted results set forth in the specification, *id.*, here, the prophetic examples set forth in the specification provide virtually nothing to be substantiated beyond the general statement that "the

[34] In a later case construing *Brana*, the Federal Circuit clarified that the "patent applicants had established the utility of claimed therapeutic compounds by presenting in vitro test results and evidence of structural similarity between the claimed and prior art compounds when filing the application." *In re '318 Patent Infringement Litig.*, 583 F.3d at 1325 n.8.

symptoms ameliorate" with treatment with the listed doses. Furthermore, assuming as the Court has that the doses listed in examples are in units of mg/day, 7.5 mg/day is not even a dose listed in the examples. It appears that to-date none of the listed dosages in the examples have been tested, and for several, it is unclear if they would be effective. *See* Richards Dep. 80:1-21 (acknowledging that it is possible but not likely that doses of 1 mg/day or 2 mg/day would be effective). Similarly, Plaintiff's reliance on the Federal Circuit's unpublished opinion in *Eli Lilly & Co. v. Actavis Elizabeth LLC*, 435 F. App'x 917, 925 (Fed. Cir. 2011), fails for the same reason, as there, the court first required that the initial statements made in the specification not be incredible.

When the applications that gave rise to the method of treatment patents were filed, they added nothing to prior art beyond highly questionable prophetic examples. Therefore, were the Court to find the claimed methods are non-obvious, it would instead find the patents invalid for lack of credible utility under the Federal Circuit's ruling in *In re '318 Patent Infringement Litig.*, 583 F.3d 1317. Although human clinical trials are not generally necessary to establish credible utility in cases involving method of treatment patents, *id.* at 1324, the utility requirement "prevents the patenting of a mere research proposal or an invention that is simply an object of research." *Id.* Here, the patent specification merely added two bare bones "examples" to the prior art. The examples each described a wide range of dosages, some of which a POSA would admittedly find implausible. *See* Richards Dep. 78:11-79:3, 80:1-9, 81:12-22 (acknowledging that the lower doses were unlikely to demonstrate efficacy). Following the submission of the application, the patentee established a particular dose, which was not listed in the examples, would actually work and amended the application accordingly. It is axiomatic that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." *Brenner v. Manson*, 383 U.S. 519, 536 (1966). The Court is not prepared to conclude that clinical trials would have

been necessary had the 7.5 mg/day dosing not been obvious. Nonetheless, Plaintiff's experts appear to acknowledge that given the nature of hot flashes, as a practical matter, clinical trials are the only way to reasonably test efficacy, and the mechanism of action of paroxetine in treating hot flashes remains unknown. *See* 12/13 (Simon) 130:7-11 ("[U]nfortunately there are no animal models, there are no blood tests, there are no other ways to assess hot flashes in women being tested with whatever kind of agents, except to ask them if they themselves have fewer hot flashes."). In conclusion, while the Court has found the claimed methods are obvious, had it not, it would instead find the patents invalid for lack of credible utility.

iii. Written Description

Defendants also allege that if the asserted claims of the method of treatment patents are not invalid as obvious, they are invalid for failure to meet the written description requirement of § 112. In order for a patent to meet the written description requirement of 35 U.S.C. § 112, the specification must "reasonably convey[] to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Ariad Pharm. Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010). "A 'mere wish or plan' for obtaining the claimed invention is not adequate written description." *Boston Sci. Corp. v. Johnson & Johnson*, 647 F.3d 1353, 1362 (Fed. Cir. 2011) (quoting *Centocor Ortho Biotech, Inc. v. Abbott Labs.*, 636 F.3d 1341, 1348 (Fed. Cir. 2011)). Defendants bear the burden of demonstrating by clear and convincing evidence a lack of written description. *Cf. Titan Tire Corp.*, 566 F.3d at 1376.

Defendants' written description argument parallels their utility argument. In short, they appear to assert if the patent is not invalid as obvious, the claimed value of the 7.5 mg/day is not supported by the patent as filed. Therefore, they assert the inventor did not have possession of the claimed invention as of the filing date. Nothing in the specifications as filed identifies dosing at 7.5 mg/day as consequential; instead, this value is listed alongside many other values that, as

explained above, are simply not plausible. Only after the patents were filed and clinical trials were conducted, did the patent applicant amend the claims to limit them to 7.5 mg/day. At the same time, the 7.5 mg/day value anchors all of the present claims. Were the Court to conclude that the patents are nonobvious, it would also conclude that the specification as it was filed does not reasonably convey to those skilled in the art that the inventor had possession of the claimed subject matter at that time.

iv. Enablement

Defendants separately challenge enablement for the '251 patent, asserting that neither the patent nor the prior art discloses how to make and use non-oral dosage forms of paroxetine mesylate or how to make dosage forms of other salts. To be enabled, the specification must teach a POSA "how to make and use the full scope of the claimed invention without undue experimentation." *Martek Biosciences Corp.*, 579 F.3d at 1378 (citation and quotation omitted).

In interpreting the '251 patent, the Court construed the term "a dosage form of paroxetine" to mean "Paroxetine or a pharmaceutically acceptable salt thereof in any of the physical forms in which paroxetine can be produced and dispensed." ECF Nos. 180 & 181. A patent need not be enabled for later-developed embodiments. *In re Hogan*, 559 F.2d 595, 606 (C.C.P.A. 1977). At the time of the invention, and still today, the only dosage forms of paroxetine were oral. 12/12 Tr. p.m. (Locker) 53:14-54:1; 12/14 Tr. (Simon) 44:7-17. Defendants have not established by clear and convincing evidence that at the time of the invention, paroxetine could have been produced in other, non-oral forms, and that those forms are not enabled. The prior art disclosed how to make and use 10 mg doses of paroxetine mesylate and paroxetine hydrochloride. Defendants have not shown by clear and convincing evidence that any other paroxetine salts were established to be pharmaceutically acceptable at the time of the invention. Accordingly, the Court finds that the '251 patent satisfies the enablement requirement.

VI. CONCLUSION

For the foregoing reasons, the Court finds that Plaintiff has not met its burden of proving by a preponderance of evidence that the '271 patent would be infringed by the sale of Defendants' ANDA products. Defendants have met their burden of proving by clear and convincing evidence that the '663 and '251 patents are invalid as obvious.

An appropriate order accompanies this Opinion.

Dated: June 9, 2017

HON. CLAIRE C. CECCHI
United States District Judge